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EDITA IUSSU SOCIETATUM RADIOLOGICARUM
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RENAL ANGIOGRAPHY IN CASES OF DELAYED EXCRETION IN INTRAVENOUS UROGRAPHY

by

Hans Idbohrn

The limitations of intravenous urography as a functional test judged by delayed excretion of the contrast agent were described in an earlier paper (IDBOHRN, 1954). As renal function is dependent on the blood supply to the kidneys, renal angiography should provide a more reliable method and in such cases complement urography.

Lumbar aortography was introduced as a clinical method by DOS SANTOS, LAMAS & CALDAS 1929 (1931). However, it was not until 1947, when the method was presented by LJUNGGREN & OLLE OLSSON mainly as renal angiography, that it found wide use in Scandinavia (OLLE OLSSON 1948, 1952, PALMLÖV 1948, 1952, RUNSTRÖM 1948, WEYDE 1948, 1951 and 1952, LINDSTRÖM 1949, DENSTAD 1952, LINDGREN 1953 and SELDINGER 1953).

The method

DOS SANTOS punctured the aorta translumbarly. This method has certain disadvantages. Thus, one is never sure whether it is the aorta or an arterial branch that is punctured. If the contrast medium is deposited selectively into the superior mesenteric artery or into one of the renal arteries, it can lead to toxic injury of the intestines or kidney. The injection of 80 per cent sodium iodide is known to have caused fatal mesenteric thrombosis (WAGNER & PRICE, 1950) and parenchymal necrosis in the kidneys (DUCUING, PONS & ENJALBERT, 1949). Organic iodine compounds such as Neo-Iopax 75 % or Diodrast 70 % have been injected into the superior mesenteric artery without serious side-effects (SMITH, RUSH & EVANS 1951, DETERLING 1952). LARSSON & PALMLÖV

Submitted for publication, March 18, 1954.

From the Roentgendiagnostic Department (Director: prof. OLLE OLSSON), of the University Clinics of Lund, Sweden.

(1952) described a case with transient reduction of urea clearance after selective contrast filling of one of the renal arteries. HARVARD (1953) reported a case of hematuria for one day and a half after the injection of a contrast medium (12 ml Neo-Iopax 75 %) directly into one of the renal arteries. At our department, transient slight to moderate renal injury has been observed in some cases after renal angiography with Umbradil 50 to 60 % (syn. Diodrast) *ad modum* SELDINGER (1953). (These cases will be reported in a later paper.)

IDBOHRN & BERG (1954) demonstrated in rabbits that considerable, mainly reversible changes occur in the renal parenchyma after the injection of Diodonum in concentrations of 17.5 per cent or more into the aorta or directly into the renal artery.

The extravascular injection of an organic contrast medium usually causes only transient pain in the left flank (RUNSTRÖM 1948, DETERLING 1952, and others). In one of our earliest cases, however, a slight effusion was seen in the left pleura.

WAGNER & PRICE (1950) recommended a test injection of a small amount of contrast medium for judging the position of the tip of the needle before the injection of the actual dose of contrast medium. This modification does not exclude the possibility of extravascular injection. LINDGREN (1953) determined the position of the tip of the needle in the aorta by means of a fine metal stylet which he introduced through the injection needle after the tip of the needle had passed the vessel wall. According to this method, the distance between the tip of the needle and the opposite wall of the aorta should be 4 to 5 mm, a distance of 1 cm or more showing that the stylet has passed into a branch or that some vessel other than the aorta has been punctured. The position of the tip of the needle in relation to the vascular region to be examined is determined by a test injection.

Hemorrhage in connection with puncture for translumbar aortography is believed to be of no clinical importance (DOS SANTOS 1931 and others). HENLINE & MOORE (1936), however, reported the death of 5 dogs from traumatic hemorrhage in connection with aortography. If the aorta is punctured at the level of the intercostal space between Th. XI and Th. XII the needle may, according to LINDGREN (1953), sometimes pass through the most inferior part of the pleural cavity and cause a small pleural effusion.

The risk of extravascular injection and the desire for more exact deposition of the contrast medium has given rise to different methods of catheterisation with the patient in the supine position, which, because of the shorter object—film distance, the high specific weight of the contrast medium, and the dorsal position of the kidneys in relation to the aorta, produces technically better films.

FARIÑAS (1941) introduced retrograde abdominal aortography with exposure of the femoral artery which was then punctured with a trocar through which the catheter was introduced into the aorta. In 1946, however, he preferred the injection of the contrast medium directly through the trocar without the use of a catheter.

GOODWIN, SCARDINO & SCOTT (1950) exposed the *lateral femoral circumflex artery*, which was then ligated and the catheter passed through it into the aorta. The method is tedious and risky.

RADNER (1948) introduced thoracic aortography with catheterisation via the radial artery. A modification of Radner's method was used by us in 1951/52 for renal angiography. According to this modification, the catheter was introduced into the descending instead of the ascending aorta.

This method is, however, no longer used because it once caused a serious circulatory disturbance of the hand in an elderly patient with arteriosclerosis. Seldinger's method (1953) is now employed; it is less time-consuming, does not require fluoroscopy and seems to be less risky. Retrograde injection of the contrast medium is also to be preferred, because it gives a more uniform filling of the aorta.

The contrast medium is injected under light general anesthesia, which decreases the

tendency to arterial spasm and facilitates the management of any toxic or allergic reactions. If, in addition, the rate of circulation of the blood is decreased by diminishing the blood pressure, more contrast medium will accumulate in the parenchyma, which may then better be studied (LINDGREN 1953). WICKBOM (1950) observed that if the blood pressure falls below 70 mm Hg, contrast medium is no longer excreted by the kidneys. In renal angiography a fairly large amount of contrast medium is delivered to the kidneys, which, if retained, might cause toxic changes in the parenchyma (cf. the importance of the duration of the application time for the degree of contrast injury by a contrast medium to the central nervous system (BROMAN & OLLE OLSSON, 1948 and 1949).

Indications

The commoner indications for renal angiography are conditions requiring investigation of the morphology of the kidneys. However, it might also prove valuable in the investigation of the function of the kidney. As far back as 1931, DOS SANTOS stressed the importance of aortography as a test of renal function. NELSON (1945) reported better excretion of contrast medium by the kidneys after aortography using Diodrast 70 % than after intravenous injection if renal function was impaired. DOSS (1946, 1947) recommended aortography for preoperative evaluation of the renal parenchyma in patients with hydronephrosis. He stressed that when the blood supply to the kidney is good, the kidney should be spared and nephrectomy reserved for poorly vascularised kidneys. WAGNER (1946), WAGNER, PRICE & SWENSON (1947) and VITT & MELICK (1947) also believed that renal angiography may yield information about the renal parenchyma. From DOS SANTOS' clinic, LJUNGGREN & OLLE OLSSON (1947) referred to two cases with ureteric stone and absence of contrast excretion on urography. Aortography showed renal circulation to be normal in one case in which ureterolithotomy produced the desired result. In the other case renal circulation had ceased and indicated nephrectomy. MELICK & VITT (1948) reported a case similar to the first of these two.

OLLE OLSSON (1948) stressed that chronic urinary stasis is one of the most important indications for renal angiography, and in 1952 he referred to some of the cases described below by the present writer.

PALMLÖV (1948) described a case of unilateral complete ureteric obstruction secondary to cancer of the bladder, in which the circulation on aortography was regarded as normal, but in which pyelostomy produced only a small amount of urine of low specific gravity. SMITH, RUSH & EVANS (1951) reported 8 cases of "completely obstructed ureters", of which they said that renal circulation was ordinary in four and normal renal function was recovered after removal of the obstruction. In the other four patients with diminished arterial supply nephrectomy showed that the renal parenchyma was severely damaged or replaced.

PALMLÖV (1952) reported the results of aortography in 42 renal cases, in 11 of which there was no excretion of contrast medium on one side at urography, and retrograde pyelography could not be performed. In one case with carcinoma of the renal pelvis and hydronephrosis the renal artery had divided into smaller irregular branches and the parenchyma showed no accumulation of contrast medium. Five cases were not verified and in the remaining 5 "the result was technically unsatisfactory".

In a preliminary report, WEYDE (1952) presented the results of 210 aortographies, of which 155 were carried out in patients with renal disease. The importance of renal angiography in the investigation of hydronephrosis was stressed, especially in those cases in which a definite diagnosis could not be obtained by urography or retrograde pyelography. The individual cases are not described, but on the basis of 23 cases he reported that the characteristic angiogram in hydronephrosis may be summarized as follows. "Atrophy of the arteries paralleling the atrophy of the renal parenchyma. At the same time possible abnormalities in the number, course, and branching of the renal vessels may be demonstrated. During the venous phase of the circulation the renal vein may be seen running in a bow-shaped arch at the base of the renal pelvis. The nephrogram indicates the atrophy of the renal parenchyma."

In his report on lumbar aortography, DENSTAD (1952) stated that atrophy and hypertrophy of the arteries must be expected in many cases to give us valuable information respecting the function of the organ concerned. Like Doss, he stresses the importance of renal angiography in the investigation of hydronephrosis for the choice of the operative method. SMITH (1953) in a résumé of his experience in carrying out 1,500 renal angiograms concluded that the true status of the renal parenchyma may be accurately determined only by renal angiography.

In addition to the above-mentioned authors there are many who, without saying why and without referring to other authors, believe that renal angiography may give information of value in such cases (GRIFFITHS 1950, SANTE 1951, BERRY, WHITE & METCALFE 1952, HAMM & HARLIN 1953).

In order to estimate properly the value of angiography for judging renal function we must select a material that permits a comparison between the findings made at renal angiography and those made before and after this examination.

At the Roentgendiagnostic Department, Lund, renal angiography has been performed on *inter alia* 22 patients in whom renal function, as judged by urography, had ceased or was poor on one side. In 19 of these the roentgen findings were confirmed with a high degree of probability.

Summary of Case Reports

a = contrast excretion preoperatively (diseased kidney)
b = contrast excretion postoperatively (diseased kidney)
0 = no contrast excretion
0^1 = » » » but accumulation of contrast medium in the parenchyma
1 = markedly impaired excretion
2 = slightly » »
3 = normal excretion

Nephrogram

0 = no nephrographic effect in the diseased kidney
1 = markedly reduced n. g. e. as compared with the other kidney
1^1 = reduced as irregular nephrographic effect
2 = slightly reduced
3 = same n. g. e. on both sides

Case No., sex, age	History and clinical finding	a	Renal angiography				Verification	
			Calibre of renal artery		Intrarenal branches Diseased kidney	Nephrogram	Operation. Histologic examination	b
			Diseased kidney	The other kidney				
1 ♀ 71	Left ureteric obstruction since 3 days before urography, probably due to stone.	0	5.0 mm	5.0 mm	fairly sparse	1	catheterization of the ureters	2—3
2 ♀ 55	Repeated left-sided attacks of urolithiasis for half a year, day before urography attack suggesting ureteric stone.	0^1	5.0	6.5	fairly sparse, slightly straight	3	ureterolithotomy	3
3 ♂ 67	Right renal tbc. for 3 years, with cystitis and stenosis of right ureteric orifice.	0	7.0	10.0	extremely sparse	0	Nephrectomy: total ren. destruct. — tub. pyonephrosis.	
4 ♂ 48	Urogen. tbc. for 1 year with pronounced cystitis and contracture of left part of bladder.	0	5.5 + 2.5 (= 5.5)	8.0	moderately reduced in number	2	Nephrectomy: most of the kidney destroyed by tbc.	
5 ♀ 43	Left-sided pyelitis periodically for 2 years. Stone at pelvo-ureteric junction. Pyuria.	0	7.0	9.0	main branches slightly straight	1	ureterolithotomy, pyonephrosis with marked hydronephrosis.	1—2
6 ♂ 39	Renal stone, 5 weeks ago passed into and lodged in the right ureter.	0	6.5	9.0	slightly straight	1	ureterolithotomy	2—3
7 ♀ 49	Right-sided pyelitis since 1944. Left-sided pyelitis since 1950. Stones in both kidneys and left ureter.	0	4.5	6.5	markedly straight main branches, small branches sparse	0—1	Nephrectomy: almost total renal destruction.	

Case No., sex, age	History and clinical finding	a	Renal angiography				Verification	
			Calibre of renal artery		Intrarenal branches Diseased kidney	Nephrogram	Operation. Histologic examination	b
			Diseased kidney	The other kidney				
8 ♂ 29	Pain in left lumbar region and hematuria after slight trauma. Anemia and increased erythrocyte sed. rate.	0	3.0 + 3.0 (= 3.5)	7.5	main branches extremely sparse, and branches strongly reduced in number	0—1	Nephrectomy: only upper pole preserved.	
9 ♀ 44	Occasional pain in region of left kidney since childhood. Nephropathia of pregnancy in 1934. Pyelitis in 1952. Pronounced left-sided pelvic dilatation.	0	4.0	6.0 + 5.0 (=6.5)	main branches straight and sparse, small branches few	1	Nephrectomy: almost total renal destruction.	
10 ♀ 61	5—6 attacks of urolithiasis during last 25 years. Cystopyelitis 1951—1952. Stones in both kidneys and left ureter. Left kidney small.	0	4.0	7.0	fairly narrow, somewhat sparse	2	ureterolithotomy	0
11 ♀ 55	Pyelitis and cancer colli uteri 1947. Rtg. therapy. Right-sided stasis for slightly more than 6 months with pyuria.	0	5.5	7.0	moderately straight main branches, small branches somewhat sparse	2	Nephrectomy: only slight renal destruction.	
12 ♀ 49	Intermittent right-sided attacks of pain for $1^1/_2$ years. Right kidney shrinking.	0	3.5 + 2.0 (= 3.5)	5.0 + 3.5 (= 5.5)	straight, sparse	1[1]	Nephrectomy: severe renal destruction.	
13 ♀ 41	Pain in right iliac fossa for several years. May 1953 tumour to right of bladder which was also involved. Cystoscopy: right ureter was not possible to catheterise.	0	3.5	6.5	straight, sparse	1[1]	Nephrectomy: almost total renal destruction.	
14 ♂ 40	For 3 months occasional attacks of ureteric stone on right side.	0[1]	8.0	7.0	no pathological changes	3	stone passage	3
15 ♂ 52	Intermittent attacks of pain on left side for 6 weeks.	0[1]	7.5	4.5 + 4.5 + 3.0+3.0 (= 5.5)	slightly straight main arteries	3	neo-ureterocystotomy	2

Case No., sex, age	History and clinical finding	a	Renal angiography				Verification	
			Calibre of renal artery		Intrarenal branches Diseased kidney	Nephrogram	Operation. Histologic examination	b
			Diseased kidney	The other kidney				
16 ♂ 53	Urinary trouble of prostate type for 3 years. Ischuria paradoxa with large amount of residual urine for 9 months. Large kidneys.	0	0	9.0	0	0	prostatectomy	0
17 ♂ 18	Traumatic rupture of right kidney three months ago.	1—2	3.0	6.0+ 3.5+3.5 (=6.0)	like main artery, marked upward disloc., vessels only in upper pole	1—2 in upper	Nephrectomy: only upper pole preserved.	
18 ♂ 43	Repeated urolithiasis for 4 years. Jan. 1951: ureterolithotomy dx. Recently often spontaneous passage of stones.	2	not exactly visualized, only slightly smaller than left renal artery	6.5+4.5 (=7.0)	slightly straight, slightly sparse	2	ureterolithotomy	3
19 ♀ 41	Recurrent pain in right lumbar region for 20 years, radiating downwards for last 2 years. Pyuria. Large kidneys.	1—2	3.0 + 3.0 (= 3.5)	7.5	straight, sparse	1—2	Nephrectomy: moderate renal destruction.	
20 ♀ 69	Tumour in right part of bladder with symptoms for 5—6 weeks. Pyuria.	0	4.0	6.0	slightly straight	0—1	pyelostomy (1 month after angiography), pyonephrosis	
21 ♀ 52	Vesico-vaginal fistula post partum 25 years ago.	0	0	5.5	0	0		
22 ♂ 42	Retentio testis until 21 years old. For 4 years seminoma testis metastasis.	0	2.0	7.0	0	0		

Discussion

In 19 of the 22 cases the results of angiography were directly comparable with the findings made at subsequent urography as well as at operation. In the nephrectomised cases the amount of functional parenchyma was estimated on the basis of the macroscopic and microscopic examinations (Summary of Case Reports, p. 337). In three cases (20, 21 and 22) certain reservation must be made regarding verification. In Case 20, the

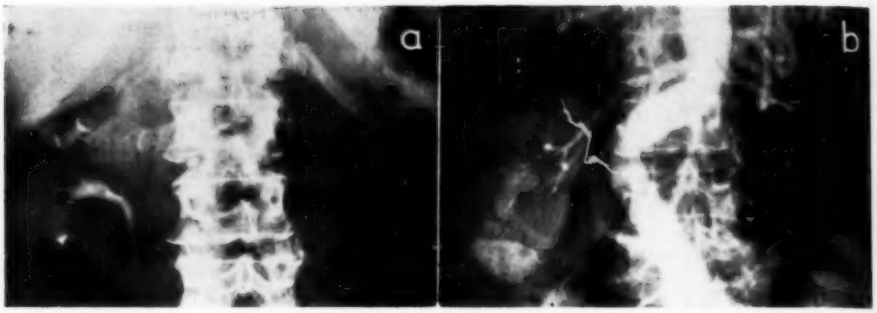

Fig. 1. Case 1. a) Urogram: no excretion or accumulation of contrast medium on left side. b) Renal angiogram: both renal arteries are of one and the same calibre. Nephrographic effect poor on left side. Markedly tortuous aorta abdominalis. c) Control urogram one month after operation: slightly decreased density of contrast medium on left side, otherwise normal.

operation was not performed until one month after the renal angiography because the effect of roentgen therapy upon a bladder cancer was first awaited. At the time of angiography the patient had pyuria, but the supply of blood to the obstructed kidney was only moderately reduced. The operation showed pyonephrosis with reduction of the parenchyma. Cutaneous pyelostomy was performed, but no clinical signs of functional recovery were recorded. The NPN, as measured on repeated occasions, was increased postoperatively, for which reason urography was not done. In Case 21 the left renal artery was completely obstructed a few millimetres from its origin. Exploration of the kidney was not considered indicated — the nature of the obstruction has not been cleared up later. In Case 22 loss of renal function on the left side was due to a palpable seminoma metastasis around the lower part of the ureter. Renal angiography revealed a practically avascular left kidney, and urograms taken over a period of 4 years showed a progressive, marked decrease in the size of the kidney suggesting total parenchymal destruction and shrinkage.

In seven of the other cases (1, 2, 5, 6, 14, 15 and 18) renal function — as judged by urography — was normal or only slightly impaired on the af-

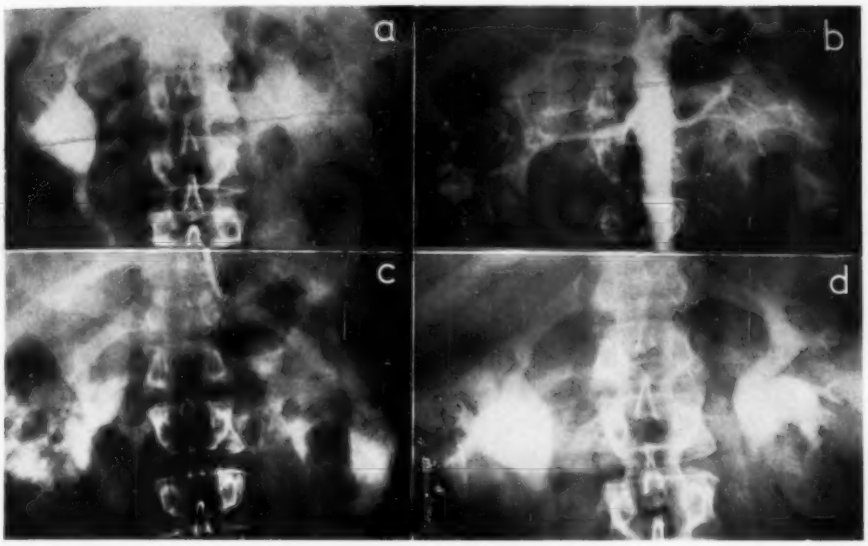

Fig. 2. Case 2. a) Urogram: accumulation of contrast medium in the parenchyma but no excretion of left kidney, which is enlarged. The right renal pelvis is fairly dilated. b) Renal angiogram: the left renal artery is slightly narrower than the right. The intrarenal arteries are straighter than usual and somewhat sparse. c) Nephrogram: good accumulation of contrast medium on both sides. d) Urogram (one year after operation): normal function on both sides. No dilatation of left renal pelvis. Right pelvis unchanged.

fected side after the ureteric obstruction had been removed. In Case 1 the obstruction was probably a ureteric stone and in Cases 2, 5, 6, 14 and 18, a stone was verified. In Case 18 the contrast filling of the renal artery was incomplete. The width of the vessel cannot be given exactly, but it was only slightly less than that of the contralateral artery and the nephrographic effect was fairly good. The width of the artery in the other 6 cases is apparent from Table I and Summary of Case Reports.

Table I

Case	Obstructed kidney	The other kidney	Difference
1	5.0 mm	5.0 mm	0 mm
2	5.0 »	6.5 »	1.5 »
5	7.0 »	9.0 »	2.0 »
6	6.5 »	9.0 »	2.5 »
14	8.0 »	7.0 »	— 1.0 »
15	7.5 »	4.5+4.5+3.0+3.0 (= 5.5)	— 2.0 »
	Mean 6.5 mm	Mean 7.0 mm	Mean 0.5 mm

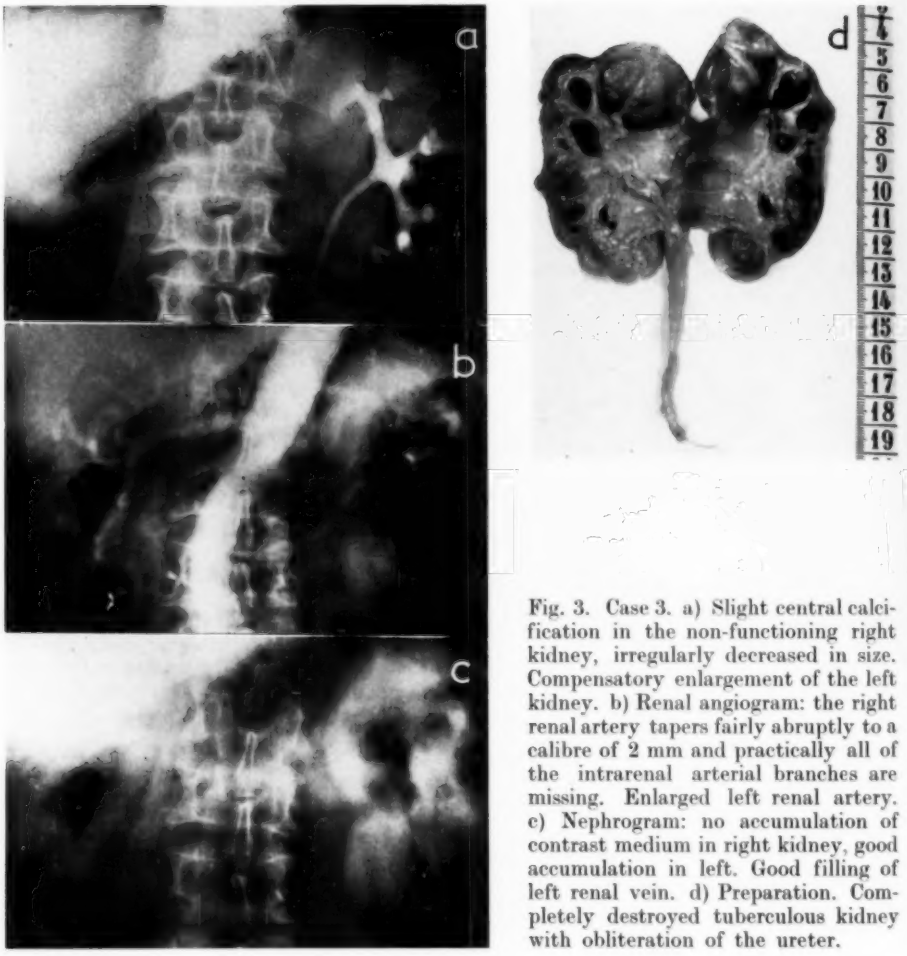

Fig. 3. Case 3. a) Slight central calcification in the non-functioning right kidney, irregularly decreased in size. Compensatory enlargement of the left kidney. b) Renal angiogram: the right renal artery tapers fairly abruptly to a calibre of 2 mm and practically all of the intrarenal arterial branches are missing. Enlarged left renal artery. c) Nephrogram: no accumulation of contrast medium in right kidney, good accumulation in left. Good filling of left renal vein. d) Preparation. Completely destroyed tuberculous kidney with obliteration of the ureter.

In Case 14, the renal artery was widest on the obstructed side. The stasis had, however, already been controlled and the urinary pathways showed no dilatation. Loss of function on urography was due entirely to the increased intrapelvic pressure. In Cases 1 and 2 (Figs. 1 and 2), the difference in the width of the vessels was negligible. The intrarenal arterial branches were, however, sparser and in Case 1 (Fig. 1 b), the nephrographic effect was decreased in the obstructed kidney. The spreading of the intrarenal arterial branches in Case 2 (Fig. 2 b) was due to the widening

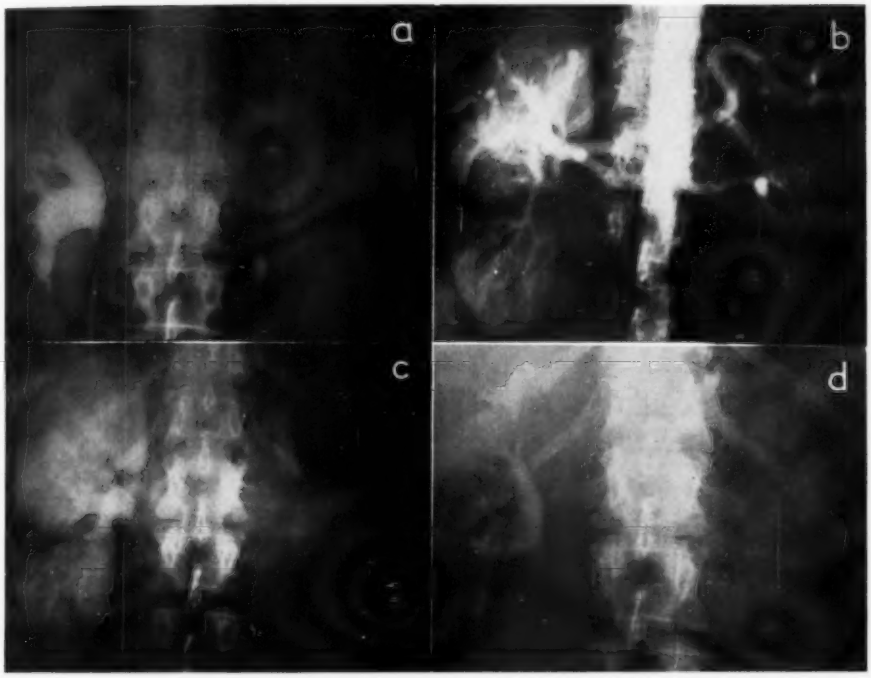

Fig. 4. Case 5. a) Urogram: large kidneys. Concrement in the upper part of left ureter and no excretion of kidney. b) Renal angiogram: the calibre of the left renal artery is slightly decreased. The interlobar arteries are fairly straight; interlobular arteries reduced in number. c) Nephrogram: only poor accumulation of contrast medium in left kidney, good accumulation in right. d) Urogram ($1^1/_2$ years after operation): impaired function and slightly dilated calyces of left kidney.

of the calyces. The dilatation of the renal pelvis, mainly extrarenal, probably had no appreciable effect on the renal parenchyma. It was reversible and 1 year later urography showed no signs of a pathologic condition. In Case 1, no signs of hydronephrosis were seen at the operation. The decrease in nephrographic effect was due mainly to the increased, intrapelvic pressure. Nevertheless, 1 month after operation the somewhat decreased density of the contrast medium seen at urography suggested slight changes in the parenchyma. In Cases 5 and 6 (Figs. 4 and 5) the difference in the width of the arteries was greater, namely 2 mm and 2.5 mm respectively. The intrarenal arteries were sparser than on the healthy side and the nephrographic effect was markedly decreased. The changes suggested moderate destruction of the parenchyma. As the main trunk was fairly

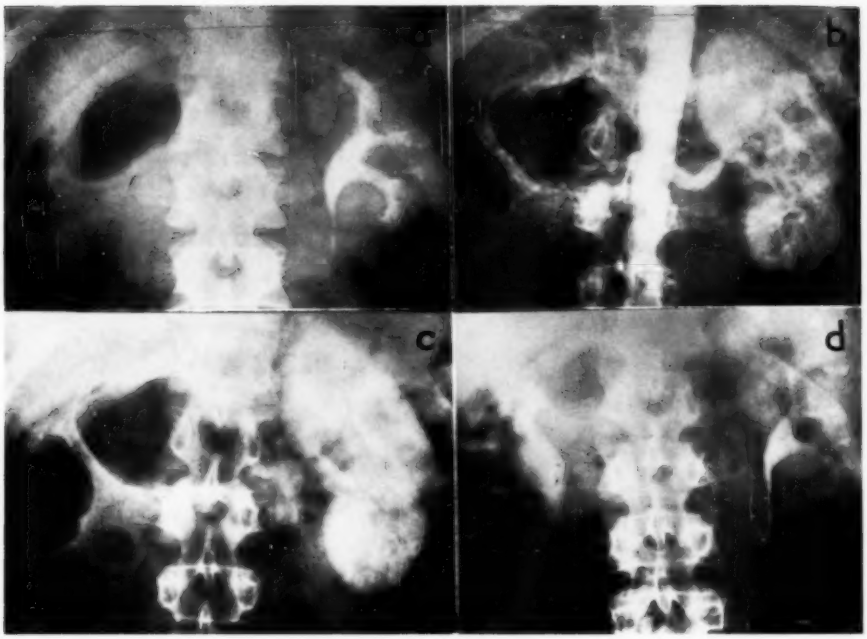

Fig. 5. Case 6. a) Urogram: no contrast excretion on right side. b) Renal angiogram: distinctly decreased calibre of right renal artery as compared with the left. c) Nephrogram: poor accumulation of contrast medium in parenchyma of the right kidney; dense accumulation in left. d) Urogram (2 weeks after operation): good excretion of contrast medium on both sides. Slight dilatation on right side.

large, it was believed that lithotomy would be followed by recovery of function. In Case 5, there was pyonephrosis with fairly marked reduction of the parenchyma. During the first few days after operation renal function had ceased, but it gradually recovered as the infection subsided. Even 18 months after operation there was still slight retardation of excretion and slight reduction in the density of contrast medium (Fig. 4 d). The calyces were still fairly dilated and were situated nearer to the surface of the kidney than usual. In Case 6, function was soon recovered but urography about 2 weeks after operation showed a moderate widening of the calyces, renal pelvis, and ureter down to the level of the operative field (Fig. 5 d).

A difference of 2.5 mm in the width of the renal arteries may thus be encountered in cases of obstruction of one ureter without loss of function being definitive. The increased intrapelvic pressure and consequent dilatation of the calyces and the renal pelvis possibly in combination

with a primary difference in the size of the renal arteries may be responsible for this difference in the width of the arteries.

In Case 15 (Fig. 11), the healthy kidney was supplied by four arteries. A rough calculation was made of the width of one single artery with the same capacity as these four together. Poiseuille's law of fluids flowing in tubes shows that the most important factor is the width of the vessel, because the flow through it increases with the fourth power of the diameter. The fall in the pressure in the blood vessels is due mainly to the resistance in the renal parenchyma. If the fall in the pressure is equal in two different-sized vessels, the width of the larger vessel need be increased only slightly for the flow through to be just as great in both vessels together. According to this rough calculation, a renal artery with a diameter of slightly more than 5.5 mm should have the same capacity as 4 arteries 4.5, 4.5, 3.0 and 3.0 mm in diameter. The artery of the obstructed kidney in Case 15 would then be about 2.0 mm larger than that calculated on the contralateral side, but the intrarenal arteries are definitely straightened and sparser (Fig. 11 b). Despite the large renal artery, then, there were signs of a slight reduction of arterial supply to the kidney. After surgical intervention on the ureter renal function was restored, but moderate hydronephrosis persisted (Fig. 11 d).

Nephrectomy was performed on 10 patients with moderate to extensive destruction of the parenchyma, on two with tuberculosis, on seven with chronic pyelonephritis associated with more or less pronounced hydronephrosis and on one with traumatic renal rupture. The width of the vessels in the cases is apparent from Table II and Summary of Case Reports.

Table II

Case	Obstructed kidney	The other kidney	Difference
3	7.0 mm	10.0 mm	3.0 mm
4	5.5 + 2.5 (= 5.5) mm	8.0 »	2.5 »
7	4.5 mm	6.5 »	2.0 »
8	3.0 + 3.0 (= 3.5) mm	7.5 »	4.0 »
9	4.0 mm	6.0 + 5.0 (= 6.5) mm	2.5 »
11	5.5 »	7.0 mm	1.5 »
12	3.5 + 2.0 (= 3.5) mm	5.0 + 3.5 (= 5.5) mm	2.0 »
13	3.5 mm	6.5 mm	3.0 »
17	3.0 »	6.0+3.5+3.5 (=6.0) mm	3.0 »
19	3.0 + 3.0 (= 3.5) mm	7.5 mm	4.0 »
	Mean 4.5 mm	Mean 7.0 mm	Mean 2.5 mm

In Case 3, one of the renal arteries was fairly large at its origin but rapidly tapered off to about 2 mm, and the intrarenal arteries were practically altogether missing (Fig. 3 b). The function had been taken

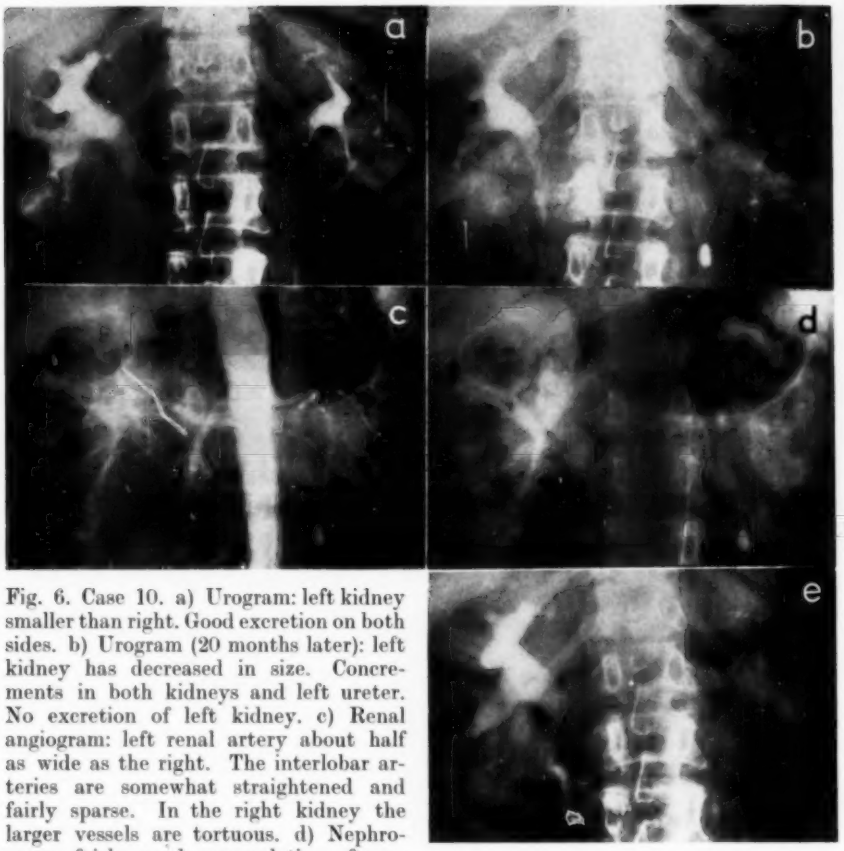

Fig. 6. Case 10. a) Urogram: left kidney smaller than right. Good excretion on both sides. b) Urogram (20 months later): left kidney has decreased in size. Concrements in both kidneys and left ureter. No excretion of left kidney. c) Renal angiogram: left renal artery about half as wide as the right. The interlobar arteries are somewhat straightened and fairly sparse. In the right kidney the larger vessels are tortuous. d) Nephrogram: fairly good accumulation of contrast medium in both kidneys; lateral outline of the right kidney irregular — pyelonephritic scars. e) Urogram (8 weeks after operation): small concrements in both kidneys. Good function of right kidney, no excretion on left side.

over completely by the compensatorally enlarged other kidney, in which vascularisation was good. In Case 4, the tuberculous process was active and the vascular and parenchymal changes considerable, but not so advanced as in the preceding case. In Case 17, angiography showed a straightened, fairly narrow artery to the upper pole, where there was vital renal parenchyma. There were no vessels in the central part of the kidney and operation revealed a large traumatic renal cyst. The remaining 7 patients had chronic pyelonephritis with more or less pronounced hydronephrosis. Angiography showed a fairly uniform picture

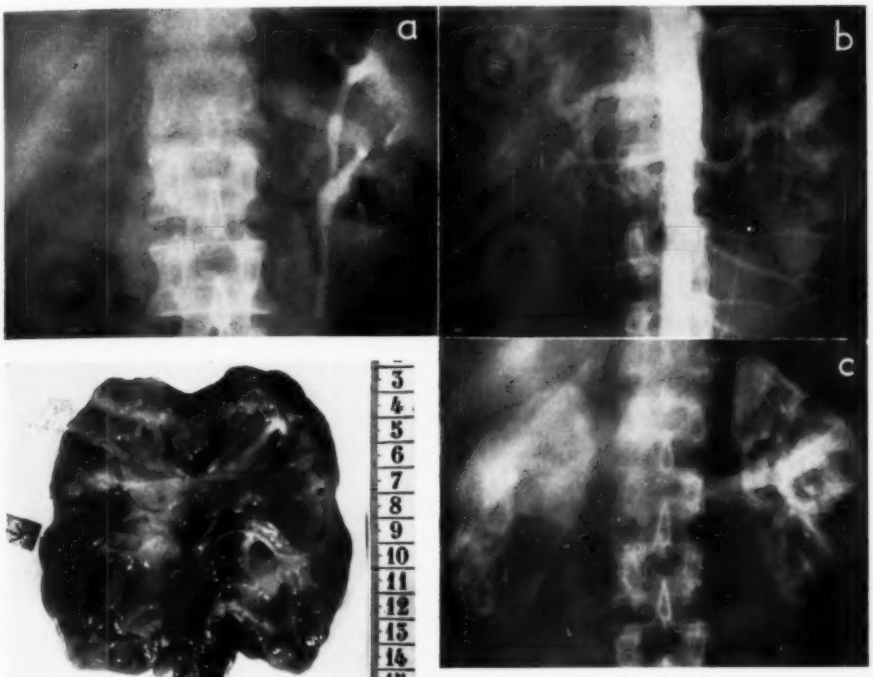

Fig. 7. Case 11. a) Urogram: the kidneys are somewhat lobulated. Good function on left side. Stasis with accumulation of contrast medium in the pelvis, but no excretion on right side. b) Renal angiogram: right renal artery straightened and narrower than the left. Straightened interlobar arteries; interlobular arteries reduced in number. c) Nephrogram: good accumulation of contrast medium on both sides. In the right kidney the major part of the demarcation between the cortex and the medulla is obliterated. In the lateral part of the kidney, diffusely outlined areas with increased accumulation of contrast medium — inflammatory foci. Left renal vein of normal appearance; the right not seen.

Fig. 8. Same case. Anatomical specimen. Considerable hydronephrosis and hydroureter. Residual parenchyma changed with inflammatory foci at those sites showing increased accumulation of contrast medium in the nephrogram.

throughout: narrow renal artery, narrow, sparse and fairly straight vascular branching in the kidney, weak and irregular nephrographic effect with only a diffuse border between the cortex and the medulla.

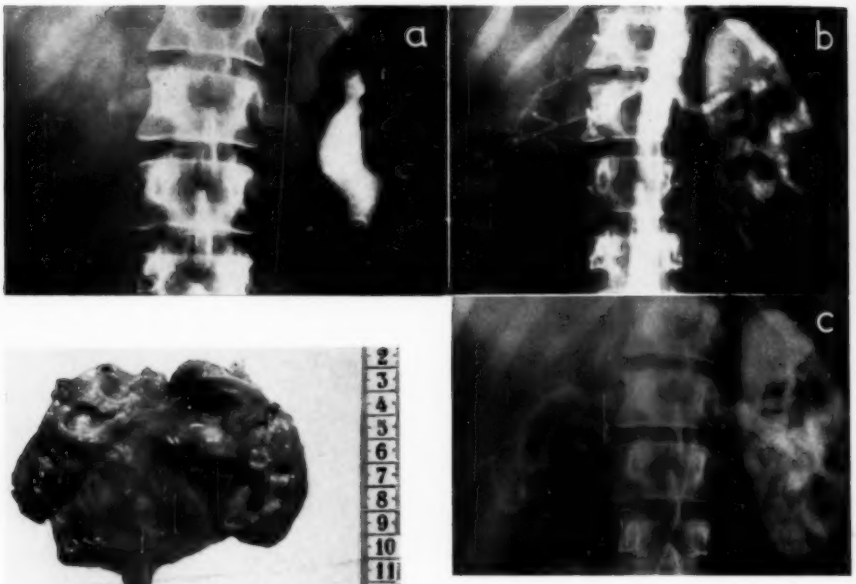

Fig. 9. Case 13. a) Urogram: deformed right kidney slightly decreased in size; no excretion of contrast medium. b) Renal angiogram: good vascularisation of left kidney. Right renal artery narrow and straightened like the larger intrarenal arterial branches, which in addition are displaced by the enlarged renal pelvis. c) Nephrogram: good accumulation of contrast medium in left kidney; left renal artery of normal appearance. Poor, irregular accumulation of contrast medium in the right kidney with lacunae at the sites of the dilated calyces. Right renal vein not seen.

Fig. 10. Preparation. Kidney decreased in size with markedly dilated pelvis. The ureter shows a stricture 4 cm below the renal pelvis, but is otherwise widened.

In Case 7, however, the renal artery was fairly well preserved, while the changes in the intrarenal vessels were marked. The other kidney was also pathologically changed with pyelonephritic scars and stones. In Case 11, there were densities with ill-defined margins in the nephrogram (Fig. 7 c) interpreted as inflammatory foci (cf. WEYDE 1952). The histologic examination showed purulent pyelonephritis with granuloma formation around necrotic tubuli. The clinical picture and urography suggested the possibility of occlusion of the renal artery in Case 12. Renal angiography,

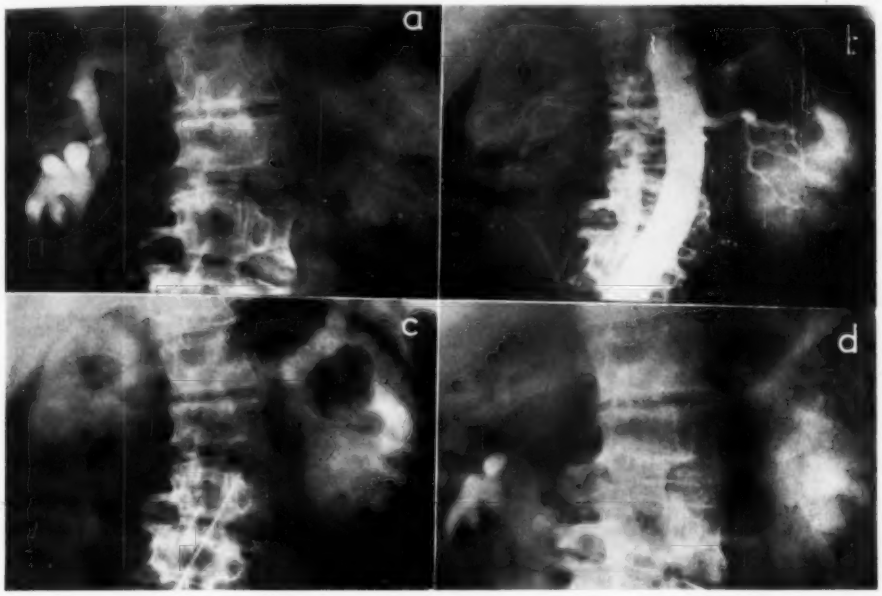

Fig. 11. Case 15. a) Urogram: left-sided stasis with accumulation of contrast medium in the parenchyma. b) Renal angiogram: one fairly wide renal artery on the left side, branching into spreading arterial branches in the kidney. The right kidney has 4 arteries, 2 of which are aberrant. c) Nephrogram: good accumulation of contrast medium on both sides. However, the accumulation is derived in part from residual contrast medium from the test injection. d) Urogram (two weeks after operation): slightly delayed excretion in left kidney, but good accumulation of contrast medium in parenchyma. Moderate dilatation of the renal pelvis and ureter.

however, showed changes due to chronic pyelonephritis. In one case (13) (Fig. 9) with signs of marked parenchymal destruction, histologic examination revealed, in addition, a small nephroma, which had not been diagnosed angiographically or at operation. The tumour was probably not of any significant importance for the diameter of the artery. Tables I and II show that in this small series the difference in the width of the artery in cases with temporary loss of function was on the average 0.5 mm, whereas the difference in cases subsequently subjected to nephrectomy was 2.5 mm. It should be observed that variations in the individual cases are considerable, so that in the evaluation of the vascularisation of the kidney not only the width of the artery, but also the changes in the intrarenal vessels must be considered.

Case 10 was of particular interest, because it showed the importance of chronic infection for progressive deterioration of renal function. From

the history as well as urographically there was evidence of pyelonephritis with stones in both kidneys (Figs. 6 a and b). The left renal artery was only slightly more than half as wide as the right, but the left kidney was also much smaller than the right. The arterial branches in the left kidney were narrow and fairly sparse as well as straighter than usual. The nephrographic effect was fairly good (Figs. 6 c and d). On angiography the contrast medium was excreted from both sides (cf. NELSON's observation 1945). It was, however, observed that in the course of some years the left kidney had gradually decreased in size. Following ureterolithotomy the infection persisted and shrinkage of the kidney advanced. The moderate destruction of the parenchyma noted on angiography had probably progressed and despite a free ureteric passage renal function had ceased (Fig. 6 e). In Case 16, the left kidney was almost completely avascular. Loss of function persisted after removal of the obstruction (prostatic hypertrophy).

In the 22 cases described the width of the renal artery in most cases was a good guide in the evaluation of renal function. However, wide variations exist for which reason renal function may readily be overestimated (Cases 7 and 10) or underestimated (Case 6). A more definite opinion about the significance of the difference in the size of the renal arteries requires a large material in which the range of variation may be determined. This necessitates an anatomic investigation on a post-mortem series and investigations on experimental animals. Such investigations are in progress and the results will be reported later in this journal.

SUMMARY

The significance of renal angiography as an important complement of urography in the diagnosis of renal function is stressed. After an analysis of the literature an account is given of the results of renal angiography in 22 cases with unilateral impaired function, 19 verified and 3 with a certain reservation concerning the verification. The importance of the calibre of the vessels as a measure of the amount of functioning parenchyma is discussed.

ZUSAMMENFASSUNG

Die Bedeutung der renalen Angiographie als ein wichtiges Komplement zur Urographie für die Diagnose der Nierenfunktion wird hervorgehoben. Im Anschluss an eine Literaturanalyse wird ein Bericht über die Ergebnisse der renalen Angiographie in 22 Fällen mit einseitiger Funktionsschädigung abgegeben; Verifikation der Schädigung liegt in 19 Fällen vor, in den übrigen 3 Fällen mit gewisser Reservation. Die Bedeutung des Gefässkalibers als ein Mass-stab für die Menge des funktionierenden Parenchymes wird diskutiert.

RÉSUMÉ

L'auteur insiste sur la valeur de l'angiographie rénale comme complément important de l'urographie pour l'examen de la fonction rénale. Après une analyse de la littérature,

il rend compte des résultats de l'angiographie rénale dans 22 cas de trouble unilatéral de la fonction rénale, dont 19 vérifiés et 3 sur lesquels il faut faire quelques réserves. L'auteur discute le rapport qu'il pourrait y avoir entre le calibre des vaisseaux et la quantité de parenchyme fonctionnant.

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FROM THE ROENTGEN DIAGNOSTIC DEPARTMENT (DIRECTOR: PROFESSOR KNUT LINDBLOM), KAROLINSKA SJUKHUSET, STOCKHOLM, SWEDEN

LOCALIZATION OF PARATHYROID ADENOMATA BY ARTERIOGRAPHY

by

Sven Ivar Seldinger

Great interest has been shown in the condition of hyperparathyroidism despite its supposed infrequent occurrence. Only in latter years has it been evident that the condition is much more common than was believed. The increased function of the parathyroids is caused either by an adenoma in one, or exceptionally two, of the glands, or by diffuse hyperplasia in all of them. Hormone producing carcinomata are extremely rare. The frequency of diffuse hyperplasia in the largest series is somewhat less than 10 %. The consequent disturbance of the calcium metabolism of the organism gives rise to two particularly striking signs: decalcification of the skeleton (mostly in form of so-called osteitis fibrosa cystica), and calcifications in the urinary tract. The radiologist contributes to the diagnosis of the disease by detecting either one or both of these features. Since it has become more common to consider hyperparathyroidism in patients with calculi in the urinary tract, the frequency with which hyperparathyroidism is diagnosed has steadily increased. HELLSTRÖM for instance, who has studied the disease since 1930, saw only 40 % of his 50 cases during the first 20 years and the remainder during the last 4 years.

There is only one adequate treatment of the disease — removal of the adenoma or subtotal resection of the hyperplastic tissue. Yet, it is often difficult to localize the enlarged gland at operation. Unfortunately, the radiologist has very little help to offer: impressions are seen in the tracheal or oesophageal wall, which, however, are uncharacteristic; in rare instances calcifications occur in the adenomata; huge adenomata have been seen projecting from the mediastinum. As, however, it has

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proved possible to localize these tumours by help of arteriography a survey of the anatomic basis of the method and a brief report of the actual cases will be presented.

Gross anatomy, situation and blood supply of normal parathyroids

The four parathyroids, if the shape of their soft tissues is not determined by surrounding structures, are oval or bean-shaped, and 3 to 6 × 2 to 4 × 0.5 to 2 mm in size. They are generally situated along the posterior border of the thyroid lobes close to the pharynx or the oesophagus,

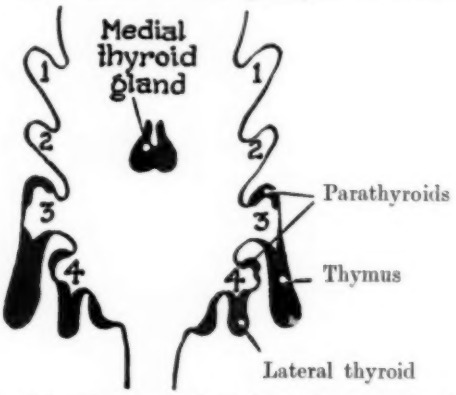

Diagram 1. The origin of the parathyroid glands from the third and fourth brachial clefts (after RIENHOFF).

or inferior to its lower poles, between the true internal thyroid capsule and the external capsule, the latter being connected with the trachea and the muscular fascia of the neck. The level of the glands varies considerably, especially that of the lower ones, which is easy to understand from the embryology (Diagram 1). The upper parathyroid (parathyroid IV) arises from the fourth pharyngeal pouch together with a portion of the thyroid, while the lower parathyroid (parathyroid III) arises from the third pouch together with the thymus. Thus, the lower gland passes the upper one during its embryologic descent and covers a much longer course as it migrates caudally with the thymus, like a knob on its upper end. It is generally deposited near the lower pole of the thyroid, but if the primordia does not separate from that of the thymus, it may descend deeply into the anterior mediastinum. Diagram 2 illustrates the distribution of 1,713 glands, found in 428 necropsies by GILMOUR. 97 % of the superior parathyroids were found close to the posterior and medial surface of the thyroid. About 83 % of the lower parathyroids were situated in the immediate vicinity of the lower pole of the thyroid or near the site

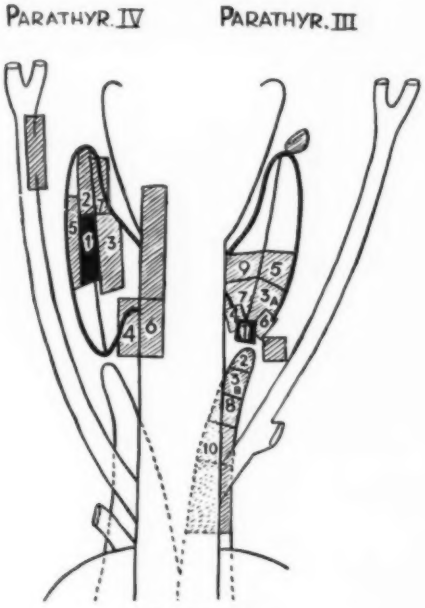

Diagram 2.

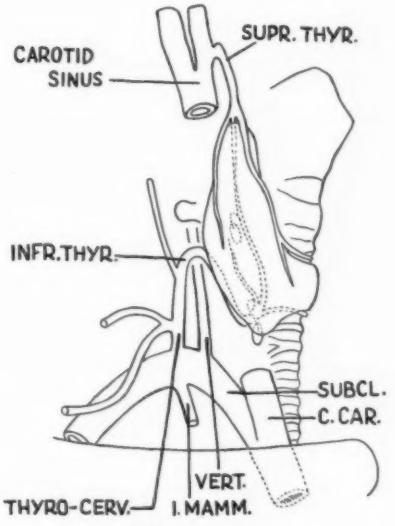

Diagram 3.

Diagram 2. Distribution of the parathyroid glands (after GILMOUR). Left: All superior glands. Right: All inferior glands. The posterior borders of the thyroid lobes have been retracted laterally. The numbers indicate the sites occupied by the glands in order of decreasing frequency. Parathyroid III: 1: 54 %. 2: 13 %. 3^{A} and 3^{B}: 7 %. 4: 6.5 %. Parathyroid IV: 1: 74 %. 2: 9 %. 3: 7 %. 4: 6 %.

Diagram 3. The arteries at the root of the neck (after GRANT: *Method of Anatomy*).

of the upper pole of the thymus, not more than 2 cm below the thyroid. Almost 15 % were distributed a little more superiorly. The mediastinal parathyroids are probably more common than appears from this, as some of them may not have been found (only 3 glands were found in 26 necropsies). Occasionally, especially in goitre, the parathyroids lie embedded in the thyroid, separated from it by a layer of the thyroid capsule. Isolated cases of true intrathyroid parathyroid glands, including adenomata, in which they are surrounded only by their own capsule, are described.

The blood supply of the parathyroids is obtained, with few exceptions, from the inferior thyroid artery, which is a branch of the thyrocervical trunk (Diagram 3). This vessel arises from the upper part of the subclavian artery, about 1 cm distal to the vertebral artery and directly above the origin of the internal mammary artery. Having given off large muscular

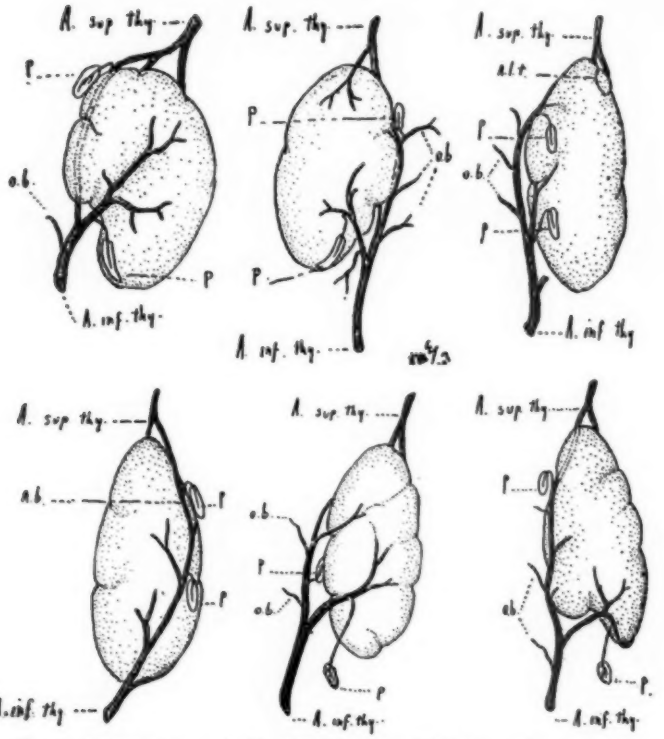

Fig. 1. Illustration of the chief types of blood supply to the parathyroid glands and their situation in relation to the inferior thyroid artery and its branches (after HALSTEAD and EVANS).

branches, it ascends under the name of the inferior thyroid artery and turns medially between the vertebral artery and the carotid sheath, reaching the middle of the posterior border of the thyroid lobe and curving downwards to the neighbourhood of the lower pole of the lobe. After giving off small branches to organs and muscles in the vicinity it divides into its terminal branches, which run mainly along the posterior surface of the thyroid. Some of these anastomose with the inferior thyroid artery of the other side, and with the superior thyroid artery, which arises from the carotid sinus and spreads mainly over the anterior surface of the thyroid.

Each parathyroid is supplied by a minute special artery, running to the hilus of the gland. The artery may arise from any branch of the inferior thyroid artery, but whatever its origin, it supplies only the gland (Fig. 1). Even if the gland lies embedded in the thyroid, the blood supply

is entirely distinct from that of the adjacent structures. The lower parathyroid artery in practically all cases comes from a prominent branch of the inferior thyroid artery. When the gland lies below the lower margin of the thyroid, which may occur rather commonly, the vessel may measure 2 to 3 cm in length. In other cases it is seldom longer than 4 to 5 mm. The upper parathyroid invariably has a short artery, which may arise from one of the main branches of the inferior thyroid artery or from an anastomosing ramus joining the superior and inferior thyroid artery. This is rather a common occurrence. "Most often however the angle at which the parathyroid vessel comes off from its parent trunk suggests strongly that its blood stream is usually from the inferior source" (HALSTEAD and EVANS, Fig. 1).

From this it is clear that, as a rule, the parathyroids are situated very close to one of the main branches of the inferior thyroid artery. MILZNER who found surprisingly many glands on the anterior surface of the thyroid capsule, emphasized that even those were in close proximity to anteriorly placed branches of the inferior thyroid vessels. The exceptions are those glands which are clearly caudal to the lower margin of the thyroid, and those which do not receive their blood supply from the inferior thyroid artery. This may occur, firstly, when the upper parathyroid artery in rare instances arises from a branch of the superior thyroid artery and secondly, when the parathyroids are situated deeply in the mediastinum and obtain their blood supply from the vessels in the vicinity of the gland.

Gross anatomy, situation and blood supply of parathyroid adenomata

The size of adenomatous parathyroids may vary from that of a normal gland to that of a hen's egg or more. In diffuse hyperplasia, at least one or two of the glands will usually reach considerable size. The form of the adenomata is to some extent dependent on neighbouring structures. If they grow in or into loose areolar tissue, they are ovoid, with a tendency to approach a spherical form as the size increases.

It appears from a paper by NORRIS, which includes a study of 322 reported adenomata, that about 85 % were at least 2 cm in their larger diameter (or "big as a hazelnut"). In BLACK's material from the Mayo Clinic consisting of 100 cases, the smaller adenomata were much more frequent. The difference is accounted for by the fact that in practically all cases in the collected series, skeletal disease was present, but only in 30 % in BLACK's material. In those 30 %, the mean size was in close agreement with that of the collected series.

"The space bounded posteriorly by the deep cervical fascia, anteriorly by the middle cervical fascia, limited above by the pharynx and extending

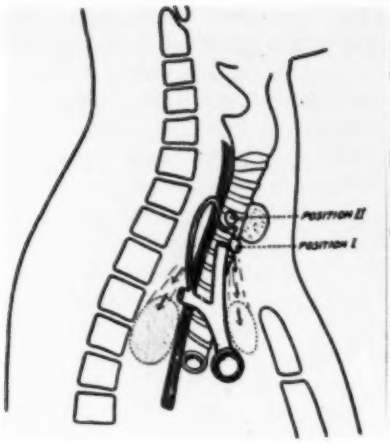

Fig. 2. Different types of downward displacement of parathyroid adenomata (after WALTON).

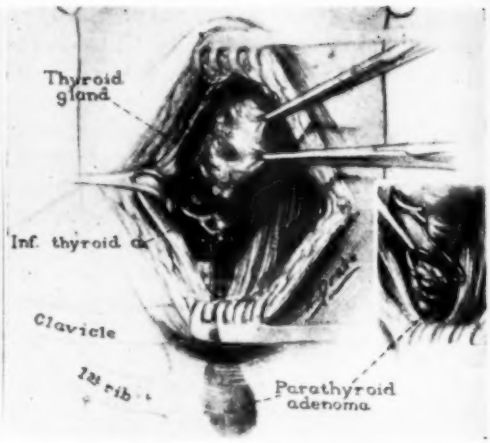

Fig. 3. Intrathoracic adenoma provided with a vascular pedicle from the inferior thyroid artery (after BLACK).

for an unknown distance downward into the mediastinum is the region for search for a parathyroid tumor" (CHURCHILL and COPE). The distribution of the adenomata is not identical with that of normal glands. In addition to the embryologic descent, adult parathyroid glands, particularly when enlarged, may be displaced caudally by gravity and intrathoracic suction (WALTON). If the gland is situated well posteriorly, the displacement is towards or into the posterior part of the superior mediastinum, and if it is situated more anteriorly, it may be displaced towards or into the anterior part of the superior mediastinum (Fig. 2). Thus, the displacement of adenomata in the superior gland is into the posterior mediastinum, and of adenomata in the inferior gland into the anterior or posterior mediastinum. They remain attached to their original arterial supply so that they are found displacing the vascular pedicle downward (Fig. 3). However, mediastinal adenomata may also develop in glands situated in the anterior mediastinum subsequent to their embryologic descent, and these are not supplied from the inferior thyroid artery. In conclusion, all adenomata in the posterior part of the superior mediastinum have vascular pedicles, while those in the anterior part may or may not have pedicles.

The reported incidence of mediastinal adenomata varies considerably. COPE, in his own material of 49 adenomata found 5 in the anterior and 4 in the posterior mediastinum, while in the numerous small series collected by NORRIS, only 7 % of the adenomata were "mediastinal". On the

other hand, in NORRIS' series more than 80 % of the adenomata were "in the region of the inferior gland", that is near to or below the inferior poles of the thyroid gland.

It is apparent from the topographic anatomy that displacement of the inferior thyroid artery or some of its large branches is likely to occur early, a fact which has been verified at operation. The parathyroid artery increases in size as the growing adenoma requires more blood and will obviously also be displaced. Even if the entire adenoma does not descend, the parathyroid artery will be stretched and displaced outside the normal distribution of the branches of the inferior thyroid artery as the adenoma expands into the tissues adjacent to the thyroid.

Technique

The contrast filling of the inferior thyroid artery was obtained by injection through a polyethylene catheter the tip of which lay in the subclavian artery, a little distal to the thyrocervical trunk. The catheter was introduced into the brachial artery after percutaneous puncture in the antecubital fossa by a technique described by the author in a previous paper. The needle was 1.5 mm in external diameter and the catheter of the same dimension or somewhat larger. 10 cc of contrast medium could be injected by hand in about 1.5 seconds or longer if desired. The films were obtained in frontal or slightly oblique projections.

Because of the close proximity of the vertebral artery, the amount and concentration of the contrast media must be carefully considered. In one case, a complication of the same type as described in cases of vertebral angiography, occurred.

A man, aged 60, with multiple bilateral urinary calculi and increased amount of calcium in the blood serum. 15 cc Umbradil 50 % were injected without any untoward effect. As the films obtained were not satisfactory, the patient was placed in an oblique position and a second injection of 15 cc given about 15 minutes later. This was immediately followed by a feeling of suffocation and generalized spasm which disappeared in a few seconds. Temporary bilateral blindness developed, with subsequent complete recovery. After a week impaired hearing on the right side developed and became permanent.

In the remaining 25 arteriographies (2 in each patient) no symptoms suggesting complications occurred, either from the injection of the contrast medium or from the puncture and catheterization. The most probable reason for the severe reaction in the above case is that the tip of the catheter was moved between the two injections and passed proximally so that the vertebral artery received the major part of the contrast medium. To avoid such an accident, the tip of the catheter should always be placed in position with the utmost care and lie immediately *distal to*

the thyrocervical trunk. This can be determined by a test exposure during the injection of very dilute contrast medium. The catheter and arm should then be immobilized until the final injection.

After the case described above (No. 4 in the series) the following amounts of contrast medium were used: 10 cc 35 %, 10 cc 50 % and 15 cc 35 %. The smallest dose was usually only enough to visualize the main trunk of the inferior thyroid artery (Fig. 5). The larger doses in most cases made the smaller branches also visible. Compression of the axillary artery was not used. Contraction round the catheter was never seen in the subclavian or axillary artery but may appear in the distal part of the brachial artery. Repeated injections were avoided, if possible.

To judge from arterial calibre only, the volume of blood flowing through the vertebral artery should be about 4 % to 5 % of that through the entire subclavian artery. Although simple hydrodynamic laws must not be applied in this case without reserve, and contraction of the brachial artery distally may reduce the flow through the subclavian artery, this will, however, give some idea of the distribution of the blood flow. The author holds the opinion, therefore, that it is unreasonable to assess the risk as larger than that of direct vertebral angiography provided the above doses of contrast medium are not significantly exceeded. Careful localization of the catheter is, however, absolutely essential.

The fact that the amount of contrast medium injected must, for the above reasons, be strictly limited, is also significant in view of the renal damage in these cases.

Case reports

Six of the patients on whom arteriography was performed were operated upon (JOHN HELLSTRÖM). In four of these cases the investigation gave correct information regarding the localization of the adenoma. Cases 3 and 4 were explored before the arteriography and no adenoma was found. They were sent to HELLSTRÖM for re-operation.

Case 1. A woman, aged 46, with multiple bilateral urinary calcifications, repeated ureteric colic, and signs of isosthenuria. The blood calcium was only slightly increased (about 11.5 mg%). No visible changes in the skeleton. Arteriography (Fig. 4) revealed that the descending part of the inferior thyroid artery, together with one of its ascending branches, formed an unusually wide bow. The branch was smoothly rounded and seemed to be displaced medially by an expanding process. At operation a parathyroid adenoma, 1 × 2 cm, was found behind the left lobe of the thyroid. The displacement of the artery was confirmed.

Case 2. A woman, aged 34, developed polydypsia and polyuria 3 years previously; also pains in the lumbar region and knees. No bone changes visible on roentgen examination. No urinary calculi. The blood calcium was high (14 mg % to 17 mg %). On arteriography (Fig. 5) the distal part of the inf. thyr. artery (or a large branch) was seen to run in a

Fig. 4, Case 1. Adenoma behind the left thyroid lobe.

Fig. 5, Case 2. Adenoma behind the right thyroid lobe. The impression in the tracheal wall is due also to a thyroid adenoma.

Fig. 6, Case 3. Adenoma below the left thyroid lobe.

circular bow, which strongly suggested that the artery enclosed an adenoma. There was a minute impression in the tracheal wall inferior to the arterial bow. At operation two rounded tumours were removed from each side. On the right side one was situated near the jugular fossa and one behind the thyroid lobe. The latter, which was surrounded by the inferior thyr. artery, proved, on biopsy, to be the only parathyroid adenoma.

Case 3. A woman, aged 52, had had repeated fractures over the previous three years. The primary diagnosis was established as osteitis fibrosa cystica. No urinary calculi. The blood calcium was about 11.5 mg %. The neck was explored but no enlarged parathyroid was found. Arteriography (Fig. 6) revealed a relatively large branch of the left inf. thyr. artery which descended considerably below the normal distribution of its branches, and finally curved laterally in a rounded bow. At re-operation a parathyroid adenoma, 15 × 10 mm in size, was found near the lower pole of the left thyroid lobe.

Case 4. A woman, aged 42, suffered over the previous three years from repeated fractures, due to osteitis fibrosa cystica. When the diagnosis was established, she had multiple calcifications in both kidneys and isosthenuria. The blood calcium was about 15 mg%. At operation one adenoma was removed from each side. Biopsy showed that they were of thyroid origin. At arteriography, as in the previous case, one branch of the left inf. thyr. artery ran vertically downwards considerably further than any other branch on either side, and finally curved laterally (Fig. 7). A further operation was performed. A structure as large as a hazelnut was found inferior to the left lower pole of the thyroid. However, it was not separate from the thyroid, and as its parathyroid origin was not clear, the entire left thyroid lobe and part of the right was removed. Biopsy revealed it to be a parathyroid adenoma surrounded by thyroid tissue.

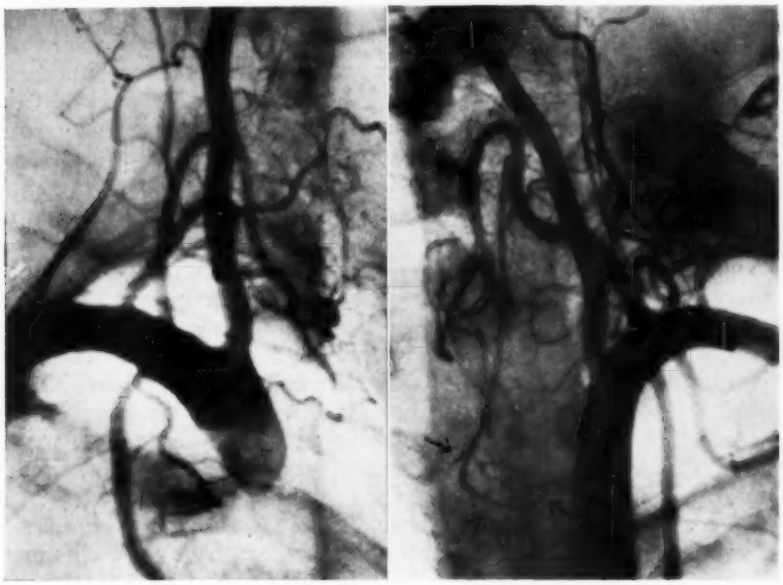

Fig. 7, Case 4. Adenoma below the left thyroid lobe.

In no other arteriogram, either in living subjects or in a series of anatomic specimens, was an arrangement of the arteries, similar to that in the above cases, seen.

In two cases no information about the parathyroids was obtained by arteriography. In one of them, $^3/_4$ of both thyroid lobes were removed after the investigation and a parathyroid adenoma of the size of a bean was found in the thyroid parenchyma. In the other patient, the whole of the right and a part of the left thyroid lobe had previously been removed. The arteriogram suggested ligated arteries on each side. On re-operation, the adenoma was found in the superior mediastinum together with thymic remnants and was connected with the left thyroid lobe by a pedicle which contained vessels.

Discussion

RADNER has reported a case in which arteriography (after catheterization from the exposed and ligated radial artery) was performed in order to investigate the presence of a parathyroid adenoma. A system of pathologic vessels was recognized, which proved to be due to metastasis from a hypernephroma. Actually, the parathyroid adenomata do not contain

vessels, numerous and large enough to be shown in this way, at least not by the present resources of arteriography. The displacement of the inferior thyroid artery and its branches, among others the enlarged parathyroid artery, is necessary for the diagnosis. A superficial thyroid adenoma may probably cause a similar picture. However, the position of the parathyroids makes it very probable that such a displacement in a case of hyperparathyroidism is, in fact, due to a parathyroid adenoma. Furthermore, any information which can be given to the surgeon as to where to seek, will be of value. The possibility of demonstrating the vascular pedicle leading to those adenomata which are situated in an abnormally low position is of special interest, as these have most often proved difficult to find. In 7 out of 9 cases sent to COPE for re-operation after unsuccessful exploration, the adenoma was found in the mediastinum. Unfortunately, those adenomata which arise in parathyroids which have descended into the mediastinum during embryologic development probably cannot be localized by subclavian arteriography unless they are supplied, for instance, from the thymic artery which generally arises from the internal mammary artery.

The contribution which may be made to the clinical diagnosis, where this is in doubt, by detection of an enlarged parathyroid by this method should be mentioned. Some authors have found a rough relationship between the size of the adenoma and the degree of hyperfunction; note BLACK's observation on the size of the adenomata in cases with and without osteitis fibrosa cystica. This, however, by no means excludes the possibility that an adenoma, large enough to be detected by arteriography may cause an indefinite clinical picture.

The indications for arteriography will depend necessarily to some extent on the surgeon's experience in the operative treatment of the disease. The first operation naturally affords the best opportunity to localize the adenoma, and the possibility of localizing the adenoma by arteriography is greater in cases which have not been operated on. As arteriography is an easy procedure, it may be desirable to perform it as a routine measure before operation, even though most of the adenomata will prove easy to find in any case. If, as the result of further experience, more restricted indications should seem advisable, the following procedure may be suitable: 1) Exploration of the neck, without resection of the thyroid or mediastinal exploration 2) Arteriography, if no adenoma is found 3) Re-operation.

SUMMARY

An anatomic survey is made from which it appears that conditions are favourable for the localization of parathyroid adenomata by arteriography via the subclavian artery; percutaneous catheterization may be employed. Displacement of the branches of the in-

ferior thyroid artery, closely adjacent to and probably supplying the adenoma should be utilized. In four out of six cases operated upon the adenoma was localized radiologically; two of these four adenomata were not found at previous operation. A complication due to the injection of an excessive amount of contrast medium into the vertebral artery is reported and discussed.

ZUSAMMENFASSUNG

Aus einer anatomischen Übersicht geht hervor, dass die Voraussetzungen für die Lokalisation von Parathyreoideaadenomen mit Hilfe einer Arteriographie über die A. subclavia günstig sind. Perkutane Katheterisierung kann bei der Arteriographie angewendet werden. Hierbei kann die Verschiebung der naheliegenden, eventuell zuführenden Zweige der A. thyreoidea inferior ausgenutzt werden. In 4 von 6 operierten Fällen konnte die Lage des Adenomes röntgenologisch bestimmt werden. Zwei dieser 4 Adenome konnten bei einer früheren Operation nicht wiedergefunden werden. Ein Fall, bei dem eine Komplikation nach Injektion einer allzu grossen Kontrastdosis in die A. vertebralis auftrat, wird mitgeteilt. Massregeln zur Vorbeugung einer derartigen Komplikation werden angegeben.

RÉSUMÉ

Il ressort d'une étude anatomique que les conditions se prêtent à la localisation des adénomes parathyroïdiens par artériographie à travers l'artère sous-clavière. L'artériographie peut se faire par cathétérisation percutanée. Le déplacement des branches de l'artère thyroïdienne inférieure qui sont en rapport étroit avec l'adénome, et probablement l'irriguent, servirait au diagnostic. Sur six cas opérés, l'adénome a pu être localisé radiologiquement quatre fois. Deux de ces quatre adénomes n'avaient pas été trouvés au cours d'une première opération. L'auteur relate et étudie une complication due à l'injection d'une quantité excessive de produit de contraste dans l'artère vertébrale.

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FROM THE DEPARTMENT OF RADIOLOGY (DIRECTOR: PROFESSOR P. FLEMMING MØLLER), UNIVERSITY HOSPITAL, COPENHAGEN, DENMARK

BRONCHOGRAPHY

Technique and Choice of Contrast Media

by

Carl E. Gudbjerg

The rapid progress of thoracic surgery during recent years has greatly increased the requirements made on bronchographic diagnostic technique.

In view of the increasing number of bronchographic examinations it is also of great importance to develop a technique which is as simple and easy as possible; it is a well-known fact that great difficulties are often encountered both at the examination itself and, later, in the interpretation of the films.

As early as 1918, JACKSON described a method by which the distribution and calibre of the bronchial tree could be studied roentgenologically *in vivo* after insufflation of bismuth powder into the trachea and stem bronchi through a bronchoscope. However, for several reasons this method did not become of practical importance, and the new epoch of diagnostic radiology was not opened until 1922, when SICARD and FORESTIER introduced Lipiodol bronchography.

During the years, various methods for the instillation of the contrast medium have been described.

The so-called subglottic or transcutaneous method with injection through the cricothyroid membrane was first introduced by French investigators and is still used. However, this method does not offer any real advantages and therefore appears to be unnecessary.

The catheter method has been employed especially for water-soluble contrast media. One of the objectives in using this method is that only part of the bronchial tree need be filled with contrast medium. As, however, a bronchographic examination is very often intended to serve as a guide in a subsequent surgical procedure, for example, in order to disclose the extent of a morbid process, we always aim at outlining the

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entire bronchial tree. We therefore regard the introduction of a catheter as superfluous, except in specially selected cases, and in children in whom the examination is carried out under general anaesthesia.

In the Department of Radiology of the University Hospital, Copenhagen, we use the transglottic technique. This method is lenient to the patient; it facilitates the examination and is fully sufficient for a good result.

A. Preparation of the patient. Half an hour before the examination, *in-patients* are given a subcutaneous injection of 1 ml of pethidine. The patients are fasting and have been informed of the examination before their arrival at the Department. *Out-patients* are instructed to take no food in the morning, and on arrival at the Department are given a tablet of 25 mg of pethidine and 5 g of syrupus codeicus fortior.

Children receive the same medication in smaller dosage but if young or uncooperative are examined under general anaesthesia.

B. Examination (duration 15 to 20 minutes). (1) Local anaesthesia: 5 drops of a 1 ‰ solution of adrenaline are added to 5 ml of a 4 % solution of cocaine. 3 ml of this mixture is poured into a de Vilbiss spray and 1 ml sucked into a Record syringe fitted with a curved blunt needle (larynx needle). Two curved swabs are placed in the remainder of the cocaine.

The patient is placed on a chair facing the examiner, and while the patient pulls on his protruding tongue with his fingers, the pharyngeal wall is anaesthetized by spraying.

Under constant control in the larynx mirror the two swabs are then pressed into both pyriform recesses, where they are held for one minute; the contents of the Record syringe are then allowed to fall drop by drop down between the vocal cords.

(2) Five minutes later the patient is placed seated on the edge of the examining couch which is slightly tilted. The patient leans towards the side which is to be examined, supporting one hand on the couch and pulling on the tongue with the other.

Under control in the larynx mirror the contrast medium is now instilled through a larynx needle from an ordinary 20 ml Record syringe. The point of the needle is placed between the vocal cords and 13 to 18 ml of contrast medium slowly instilled, while the patient first leans a little backwards and then a little forwards. After cessation of the instillation the couch is tilted further (about 60°) and the patient placed first in the lateral, then in the semiprone, and finally, for a few moments in the semidorsal position. These manipulations usually result in filling of the entire bronchial tree.

(3) In rapid succession exposures are then made with the patient in the following positions:

(a) Lateral (about 15° Trendelenburg)
(b) Prone do.
(c) Dorsal do.
(d) Sitting (lateral view)
(e) Sitting (anteroposterior view).

After-Treatment. Following the introduction of the addition of sulphonamides to the iodized oil we have attempted postural drainage, the patient being at once placed in the full Trendelenburg position and requested to cough and expectorate. Preliminary experience suggests that it is possible in this way to eliminate a considerable portion of the contrast medium.

Food and fluids are withheld for two hours after the examination because of the local anaesthesia. Otherwise, no after-treatment is given.

Contrast Media

One of the most important problems in bronchography is undoubtedly the choice of the contrast medium. For a number of years iodized oil was almost universally employed. This agent offers so many advantages that it must still be supposed to be the most commonly used contrast medium. Its contrast effect has so far remained unsurpassed, and as it causes little local irritation, only light local anaesthesia is required. On the other hand, alveolar filling occurs relatively easily, and the agent is but slowly eliminated.

In 1948, MORALES and HEIWINKEL introduced a new water-soluble contrast medium, Umbradil-Viscous B, and shortly afterwards, FISCHER (1948) described a similar agent, Joduron B.

These substances offer the unquestionable advantage that the radiopaque component rapidly disappears. On the other hand, it soon became evident that the viscous component — carboxymethyl cellulose — is not eliminated, but remains unchanged in the alveoli and bronchi for months.

In experimental studies on rats, HELLSTRÖM (1953) compared Umbradil-Viscous B and Joduron B. The contrast media were introduced through a catheter under anaesthesia. The animals were killed after intervals of 2 days, and 1, 2, 3 and 6 months respectively, and the lungs examined macroscopically and microscopically. Even though the results of these experiments can scarcely be taken to apply in every respect to man, they nevertheless provide some useful information. Minimal amounts of carboxymethyl cellulose could be demonstrated in the animals which had been given Umbradil, but there were no signs of foreign-body reaction.

In the rats which had received Joduron, carboxymethyl cellulose was present in considerably larger amounts and, around the substance, distinct irreversible changes with induration and chronic inflammatory reactions could be demonstrated. From this view point, the water-soluble media scarcely offer any advantage over iodized oil.

Moreover, the water-soluble media do not give quite as good a contrast effect as iodized oil, and as they cause greater local irritation require deeper anaesthesia; for these reasons we have so far preferred oil to Umbradil-Viscous B and Joduron B.

We have always regarded it as a considerable drawback however that the use of iodized oil so often results in filling of the alveoli. Once this has occurred, the contrast medium cannot be removed by drainage or otherwise.

Filling of the alveoli is undesirable because the retention of the radiopaque oil causes difficulties in the interpretation of the bronchograms,

a. b.

c.

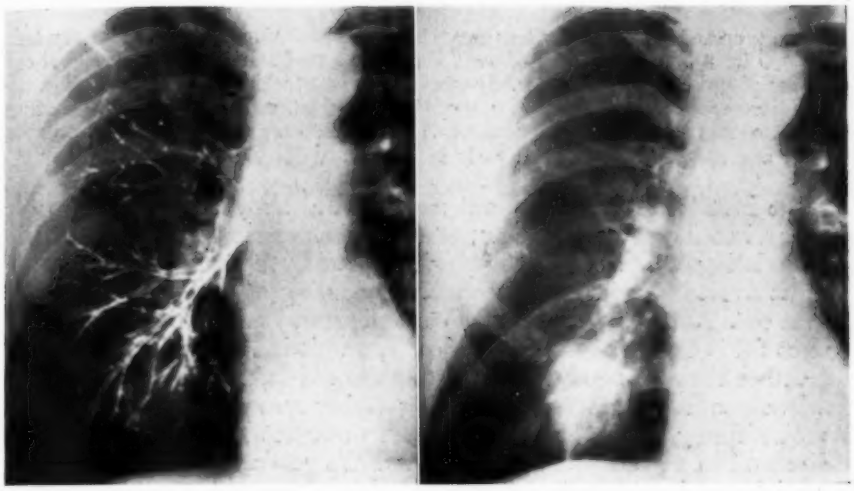
Fig. 1. a. Right bronchography with a suspension of 7 g sulphathiazole in iodized oil. b. 1 hour later. c. 48 hours later.

detracts from the value of subsequent examinations, and involves the risk of iodism and irreversible pulmonary changes.

We have therefore tested a number of new contrast media.

Dionosil and Dionosil Oily are both water-soluble, although the latter is a suspension in peanut oil. The iodine content is 40 and 34 per cent, respectively. We are under the impression that the introduction of these media does not mark any big step forward. Both cause greater local irritation than iodized oil and their contrast effect is distinctly inferior. Accordingly, we have abandoned the use of these agents.

For therapeutic reasons, DORMER, FRIEDLAENDER and WILES



a. b.

Fig. 2. a. Right bronchography with a suspension of 5 g sulphadiazine in iodized oil. b. 48 hours later.

(1945) added sulphonamide to iodized oil used in the treatment of inflammatory diseases of the lung. They noticed that alveolar filling rarely occurred, and that it was possible for the patients to cough up the greater part of the contrast medium in the course of a few hours or days.

HOUGHTON and RAMSAY (1951) obtained similar results after the addition of 10 g of sulphanilamide to 20 ml of iodized oil.

RATJEN (1954) made the same observation, but used only 3 g of sulphadiazine to 20 ml of iodized oil.

In January 1954 we started a series of experimental studies in which sulphonamide in various concentrations was added to iodized oil used for bronchography.

A total of 50 such bronchographic examinations have so far been carried out:

5	with	the	addition	of	10	g	sulphathiazole	to	20	ml	iodized	oil.
10	»	»	»	»	7	»	»	»	20	»	»	»
11	»	»	»	»	5	»	»	»	20	»	»	»
18	»	»	»	»	5	»	sulphadiazine	»	20	»	»	»
6	»	»	»	»	3	»	»	»	20	»	»	»

The suspensions were prepared in the dispensary of the University Hospital.

Preparation of the suspensions. As iodized oil is not stable to heat, the suspensions must be prepared with due aseptic precautions. Sulphadiazine is sterilized by dry heat at 140° C for 3 hours. On a slip of weighing paper 5 g of sulphadiazine is weighed out and then placed in a sterile mortar. By means of a pestle, which must also be sterile, the sulphadiazine is ground with about half of the iodized oil, while the remainder is added during constant stirring. The preparation is poured into a glass jar fitted with a glass stopper and should be stirred vigorously before use.

The instillation is carried out as described above, but owing to the higher viscosity of the medium, the examiner must be more careful in manipulating the patient. However, by placing the subject in the position as previously described, satisfactory filling of the entire bronchial tree is obtained in the course of 3 to 5 minutes. The fact that the alveoli do not fill is due to the higher viscosity, and it is therefore important to remember that *the medium must not be warmed before use*, but should be used at room temperature. Warming before use may easily result in alveolar filling, and then the medium does not differ from ordinary iodized oil in regard to the elimination. We prefer the suspension with 5 g sulphadiazine as we find that it possesses the most appropriate degree of viscosity. This suspension produces good filling of the entire bronchial tree without any tendency to alveolar filling. The contrast medium is coughed up within a short time which varies from some hours to a few days. The addition of sulphonamide does not increase the irritancy of the oil, the contrast effect is not impaired, and we have not observed any toxic side-reactions or other complications in the use of these media.

It is our preliminary impression that, owing to its rapid elimination, a suspension of sulphonamide in iodized oil is the best contrast medium for bronchography at present in existence, and thus represents a very considerable advance in diagnostic radiology of the lungs.

SUMMARY

The technique of instillation of contrast medium for bronchography is described. A variety of new contrast media have been tested. A suspension of 5 g of sulphadiazine in 20 ml of iodized oil is considered to be the best contrast medium so far available. This agent does not cause local irritation, its contrast effect is good, and toxic side-reactions have not been observed. Alveolar filling is rare (if the medium is not warmed before use) and rapid and its complete elimination may be effected by coughing.

ZUSAMMENFASSUNG

Die Instillationstechnik des Kontrastmittels für die Bronchographie wird beschrieben. Zahlreiche neue Kontrastmittel sind untersucht worden. Eine Suspension von 5 g Sulfadiazin in 20 ml Jodöl wird als das beste bisher zugängliche Kontrastmittel angesehen. Dieses Agens erzeugt keine lokale Irritation, seine Kontrastwirkung ist gut und toxische Nebenwirkungen sind nicht beobachtet worden. Die Ausfüllung der Alveolen

geschieht in dünner Schicht (falls das Kontrastmittel nicht vor dem Gebrauch angewärmt wird) und sehr hastig; die völlige Eliminierung des Kontrastmittels kann durch Husten hervorgerufen werden.

RÉSUMÉ

L'auteur décrit la technique d'instillation du produit de contraste pour bronchographie. Plusieurs nouveaux produits de contraste ont été mis à l'essai. C'est une suspension de 5 g de sulfadiazine dans 20 cc d'huile iodée qui est considérée comme le meilleur produit de contraste dont on dispose actuellement. Ce produit ne cause aucune irritation locale, son effet de contraste est bon et on n'a pas observé d'effet secondaire toxique. S'il n'est pas réchauffé avant l'emploi, il remplit rarement les alvéoles et est complètement éliminé par la toux.

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FROM THE MEDICAL DEPARTMENT (DIRECTOR: DOCENT GUNNAR LINDGREN) OF THE STREET OFFICE OF STOCKHOLM, AND THE ROENTGEN DEPARTMENT (DIRECTOR: PROFESSOR ERIK LINDGREN) OF SERAFIMERLASARETTET, STOCKHOLM, SWEDEN

HEART VOLUME DETERMINATION ON MICROFILMS

by

Gunnar Lindgren and *Sven Odén*

In roentgen examinations of the heart it is important to study the cardiac pulsations, the total volume and the size and shape of the different chambers as well as the course and appearance of the great vessels. The posterior-anterior (p-a) view generally gives a good deal of information about these factors. The diagnostic possibilities, however, increase considerably when the heart is examined in more than one projection.

Several of the details indicated may be assessed with sufficient accuracy on miniature chest films provided that these are of high quality and the examiner is experienced in cardiac radiology. Moreover, lateral projections are essential in estimating the heart volume, because calculations of the total volume from the size of the heart in only one projection are often quite fallacious.

In comparison with the standard roentgen examination of the heart the microfilm technique has many advantages. The method saves film and the examination may be carried out by mobile units near the centre of employment thus saving time for both the employer and the employee. Another advantage is that the examination may be performed by a technician instead of a radiologist. Several investigations have been carried out and published about the possible value of mass miniature radiography in the detection of cardiac disease. The opinions of the various workers have been rather divergent. Many authors are inclined to attach no, or only a rather limited, value to the microfilm method, indicating that only very few cases of cardiac disease will be detected in proportion to the number of persons examined. In most of these surveys, however, only the posterior-anterior projection had been used, hence no heart volume determination was possible. The size and the quality of the films varied and few of the examiners had been specially trained in the radiology of the heart. Another important factor which appears to have been overlooked in some of the publications, is that when a mor-

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bidity declines below a certain low value a mass examination has to be directed to comprise only those groups of individuals who are particularly exposed to the disease in question. The proportions between the work performed and the result obtained will otherwise be incongruous.

An adequate planning of a mass radiography campaign implies acquaintance with the accuracy of the method used and its facilities for disclosing disease. The possibilities of diagnosing cardiac disease on microfilm from the changes in the contours of the heart and the great vessels have been and will be closely studied in other connections hence we need not deal further with this part of the problem here. We have, however, been able to find only one reference to the determination of the heart volume on microfilm (GUBNER and UNGERLEIDER). The method reported in this paper differs in so many respects from the technique now common in Sweden that we consider the matter worthy of further study, the main reason being that the determination of the heart volume forms an important part in the selection and control of workmen in occupations requiring physical strength. The reader may be reminded of the work by SJÖSTRAND et al. on the possibilities of tracing early cases of heart disease by simultaneous determinations of the heart volume and the total body content of haemoglobin.

Material

The material for this investigation comprises persons who have made application for employment to the Street Office of Stockholm as well as those already employed but referred for roentgen examination for other reasons, *e. g.* exposure to silica dust or other industrial hazards. The majority of those examined were men who were accustomed to and employed in heavy manual labour.

We have used determination of the heart volume on microfilm as a routine method since September 1951. After sufficient experience concerning technical details had been collected, 150 cases consisting of 136 males and 14 females, were chosen at random for a close analysis of the method. The selection was made from a material comprising about 1,000 volume estimations.

The age distribution of the cases studied in detail was as follows.

Age in years	Number of cases
< 20	13
20—29	44
30—39	54
40—49	20
50—59	15
$\geqq 60$	4
Total	150

Fig. 1. Support for taking radiograms in the lateral position.

Technique

In the microfilm examinations a slightly modified mass radiography apparatus of standard type is used. The apparatus consists of a Philip's stand and a DIK 1000 unit manufactured by Schönander.

Heart volume estimation involves examination in two projections at right angles. To obtain well-exposed radiograms of the sagittal cardiac plane a higher voltage as compared with most mass radiography examinations of the standard type must be used. We therefore replaced the standard roentgen tube by a Super-Dynamax.

The exposure time in the p-a projection varied from 0.28 to 0.36 seconds at 300 mA and 90 to 100 kV. The corresponding values for the lateral view amounted to 1 to 1.5 seconds at 200 mA and 95 to 105 kV.

Gaevert's Scopix film (7.5 × 7.5 cm) was used; the developing time was 7 minutes.

It is impossible to adjust the position of the patient by screening when taking radiograms on microfilm to determine the sagittal diameter of the heart. In order to prevent oblique projections, it soon proved necessary to construct a special support on which the anterior thoracic wall of the subject examined rested during the exposure (Fig. 1).

A barium contrast medium was regularly used in the same way as in ordinary roentgen examinations so as to visualize the oesophagus with the vascular and cardiac impressions.

In the experiments to investigate the value of the mass radiography technique as a method for cardiac volume estimations a number of the microfilm examinations were made at the same time as the ordinary roentgen investigations employing the technique described by AXÉN, LINDGREN and MALMSTRÖM (1946).

Determination of the volume of the heart from its longitudinal, transverse and sagittal diameters. From the length (L), breadth (B) and the sagittal diameter (S) in the roentgenograms, the cardiac volume may be calculated according to the formula $k \times L \times B \times S$. In the ordinary teleroentgen examination with a distance of 1.5 m between the focus of the tube and the film, the value of k is 0.42. In our microfilm examinations the distance between the focus and film was 80 cm, hence the fac-

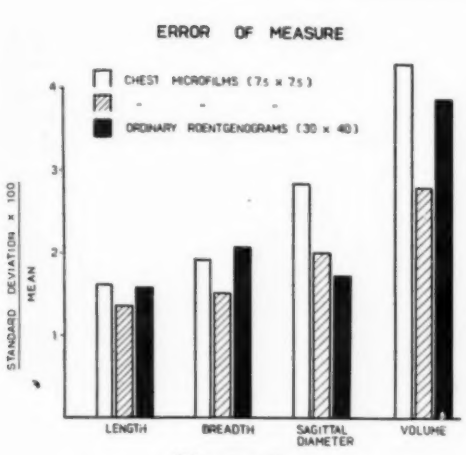

Diagram 1.

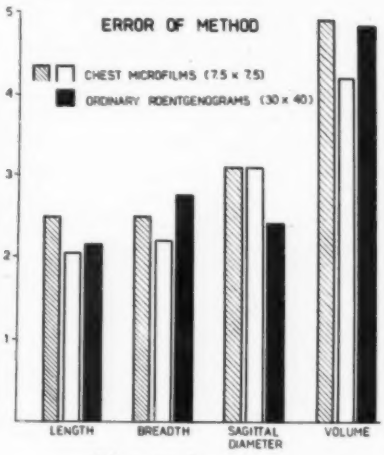

Diagram 2.

Diagram 1. Comparison between determinations on micro- and on ordinary roentgen films. The white columns (□) denote that the focusing and the exposure in the microfilm apparatus has been carried out by a technician, whereas the measuring has been performed by a roentgenologist (O.). In the other cases (▨, ■) both the focusing, exposing and measuring have been made by a roentgenologist (O.).

Diagram 2. Comparison between determinations on micro- and ordinary roentgen films. All the micro-radiograms were taken by a technician and the ordinary ones by a roentgenologist (O.). The standard radiograms (■) and one of the series of microfilms (□) have been measured by roentgenologist O., the other series (▩) by roentgenologist G.

tor k had to be recalculated; taking the altered circumstances into account, a k value of 0.35 was obtained. Before the above formula was used, the reduction in the microfilm optics was allowed for by converting the measurements into the corresponding values obtained from the fluorescent screen.

Control determinations on a phantom showed close agreement with the k value of 0.35 obtained theoretically.

Accuracy of Method

Error of measure. The heart diameters were measured in millimeters directly on the microfilms without magnifying apparatus. As a rule this procedure did not prove difficult.

The error of the single determination (σ) of the diameters on microfilm has been directly calculated out of a series of double measurements on films from 50 examinations. Another series of measurements were

made on ordinary roentgenograms from the same individuals and the diameters assigned in half centimeters. Each measurement was made twice, the roentgenologist measuring the second determination not knowing the result of the first. From the values of the double determinations thus obtained the standard deviation was calculated according to the method described by DAHLBERG. Diagram 1 shows that the standard deviation in the microfilm technique — as well as in ordinary roentgen examinations — amounts to 1 to 2 per cent of the measured mean diameters. The error of measure is thus about the same in the two methods.

Error of method. The error of the microfilm method has been calculated from a series of 120 complete examinations on 60 subjects, each one having been examined twice within an interval of about one hour. The focusing and the exposure were made by a technical assistant, the measuring on the films by two experienced roentgenologists. Each measurement was made without knowledge of the results of other measurements on the same subjects. The error of the single determination (σ) as a percentage of the average (the coefficient of variation) was then calculated from double determinations in the same way as the error of measure. It was found to be approximately 2 as regards the length and the breadth of the heart in the p-a projection, 3 in the sagittal diameter and 5 so far as the volume of the heart was concerned. The results of the two roentgenologists were almost in complete agreement. A comparison with a series of 80 estimations obtained by ordinary teleroentgen examinations performed by one of us (O.) on 40 cases shows that the error of method in ordinary roentgen and in microfilm technique is practically the same.

Comparison between simultaneous determinations of the heart volume on the same subjects by means of microfilm and ordinary teleroentgen technique. Fifty subjects were examined by means of the microfilm technique, the focusing and exposing being made by a technician. Immediately after each exposure the volume was determined by means of the teleroentgen technique. Another microfilm examination was then performed, by roentgenologist O. The cardiac diameters were measured twice on the microfilms by O. and once by roentgenologist G. The teleroentgenograms were measured once by O. and once by G. Diagram 3 illustrates the relationship between the microfilm values thus obtained (ordinate) and the corresponding teleroentgen values (abscissa) and indicates that there is little discrepancy between the two methods.

The regression heart volume—body surface was also calculated on the 50 persons studied. In this respect, too, good agreement between the two methods was obtained, the regression equation for microfilm tech-

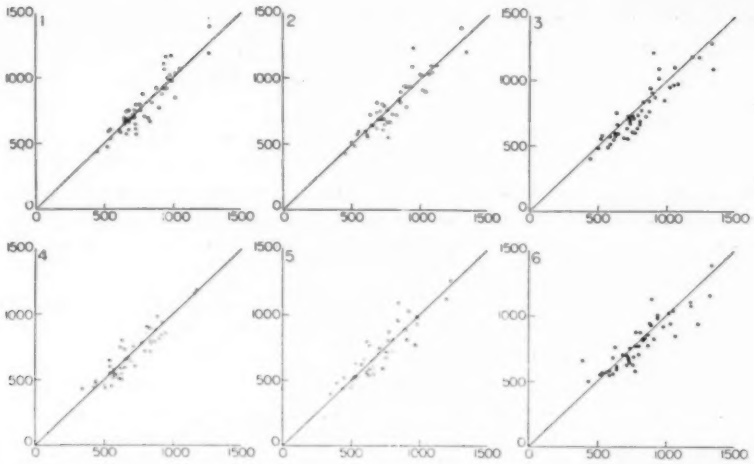

Diagram 3. Simultaneous determination of the heart volume in ml in microfilms and ordinary roentgenograms. *Ordinate* — microfilms. *Abscissa* — standard roentgenograms. The microfilms in the upper line (1—3) were taken by roentgenologist O. and in the bottom line (4—6) by a technician. All the ordinary roentgenograms were taken by O. Nos. 1, 2, 4 and 5 were measured by O., 3 and 6 by G. The indication ○ denotes that the measuring in the microfilms as well as in the standard roentgenograms was performed by roentgenologist O., the indication ● that roentgenologist G. had made the measurements.

nique being: $y = -504 + 677\ x$ and for teleroentgen technique $y = -463 + 673\ x$, where y signifies the heart volume figure in ml and x the body surface in m^2.

For advice on statistics we are indebted to Docent L. Goldberg, Department of Pharmacology, Karolinska Institutet, Stockholm. The investigation has been supported financially by the Research Fund of the Town Council of Stockholm.

SUMMARY

The advantages of chest microfilm technique as compared with standard teleroentgenology, are, inter alia, the saving of films and the fact that a technician is able to carry out the examination near the place of employment. The Rohrer-Kahlstorf method for heart volume estimation applied to microfilm technique has been elaborated. It shows the same degree of accuracy as the corresponding teleroentgen measurements. In both cases the error of method (σ) scarcely amounts to 5 % of the heart volume.

ZUSAMMENFASSUNG

Die Vorteile der Thoraxschirmbildtechnik im Vergleich mit der üblichen Teleröntgenologie sind u. a. Filmersparnisse und die Tatsache, dass ein Techniker die Unter-

suchung in der Nähe des Arbeitsplatzes ausführen kann. Die Rohrer-Kahlstorfmethode zur Bestimmung des Herzvolumens ist unter Benutzung der Mikrofilmtechnik sorgfältig durchgeführt worden. Sie zeigt die gleiche Genauigkeit wie die entsprechenden Teleröntgenmessungen. In beiden Fällen beträgt der Fehler der Methode kaum 5 % des Herzvolumens.

RÉSUMÉ

Les avantages de la radiophotographie thoracique par rapport à la téléradiographie standard sont, entre autres, l'économie de films et le fait qu'un manipulateur peut procéder à l'examen près du lieu de travail. Les auteurs ont mis au point l'application à la technique des microfilms de la méthode de Rohrer-Kahlstorf pour l'estimation du volume du cœur. Elle donne le même degré de précision que les mesures correspondantes en téléradiographie. Dans les deux cas, l'erreur avec cette méthode atteint à peine 5 % du volume du cœur.

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FROM THE DEPARTMENT OF PHYSICAL CELL RESEARCH, KAROLINSKA INSTITUTET AND THE OTO-LARYNGOLOGIC CLINIC OF SABBATSBERGS SJUKHUS, STOCKHOLM, SWEDEN

MICRORADIOGRAPHIC STUDIES OF THE AUDITORY OSSICLES (MALLEUS AND INCUS) AND OF THE OSSEOUS LABYRINTH

by

K. Karlsson, A. Engström and *H. Engström*

Soft roentgen ray microradiography of thin sections of bone tissue has proved to be of great value in studying the distribution of mineral salts in different bone structures (AMPRINO and ENGSTRÖM, 1952). In a cross-section of the diaphysis of a long bone, for example, it may be shown by microradiography that the content of mineral salts varies from one haversian system to another and that the degree of mineralization may be correlated with the varying uptake of radioactive isotopes. Those structures which have the smallest content of mineral salts show the highest uptake of such radioisotopes as radiophosphate, radiocalcium, radiosulphate and radiostrontium. Haversian systems of low mineralization in addition also show a high *in vitro* exchange of radioisotopes (ENGFELDT and HJERTQUIST, 1954). Most probably these structures (haversian systems) have an important physiologic function in the regulation of the ionic milieu in the body.

In previous investigations compact and spongy bone tissue from the long bones, vertebra and skull have been extensively investigated. The present investigation is intended to show the distribution of the mineral salts within the auditory ossicles of the middle ear and the hard bone tissue found in the osseous labyrinth.

The material and its preparation

The osseous labyrinth was obtained at autopsy. Sections of known orientation, about 2 mm thick, were prepared by sawing and embedded in thermoplast or methylmethacrylate. After the plast had solidified the sections were ground, first on emery

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paper to a thickness of about 300 microns and then polished on special glass plates to a final thickness of 100 to 200 microns. The thermoplast was then removed by absolute alcohol. Sections from the inner ear of rabbit were prepared in the same way.

Theoretical considerations on the roentgen technique for the histochemical determination of mineral salts

Microradiograms may now be registered with a resolution which is better than 0.5 micron (ENGSTRÖM, 1953, ENGFELDT and ENGSTRÖM, 1954). The main obstacle for obtaining a high resolution is the photographic emulsion. The thin ground section is placed in direct contact with a photographic emulsion and a shadow image to a 1 : 1 scale produced. This image is enlarged by photomicrography. The possible magnification depends on the sharpness of the original roentgen image. The image definition in turn depends on the geometric conditions *i. e.* the size of the focal spot of the roentgen tube, the thickness of the sample and the distance of sample-film from the target. In the arrangement used in the present experiments, the geometric unsharpness (penumbra) was 1 micron for a 100 micron thick section. Due to the high contrast of the object it is easy to obtain high resolution. The geometric conditions were thus sufficiently good for these experiments. Of course it is easy to increase the definition in the image by increasing the distance from the focus but the exposure times then become very long. It is in fact of little use as the limiting factor in the resolution in this case lies rather in the photographic emulsion than in the beam geometry.

The fine-grained photographic emulsions used, Lippmann-film, Eastman Kodak Spectroscopic Plates 548 or 649, and Kodak Maximum Resolution Plates are capable of resolving more than 1,000 lines per mm. This high resolution is not obtainable with all emulsions, as they vary from one batch to another. Resolution tests must therefore be carried out. Fig. 1 shows a microradiogram of a silver grid (kindly supplied by

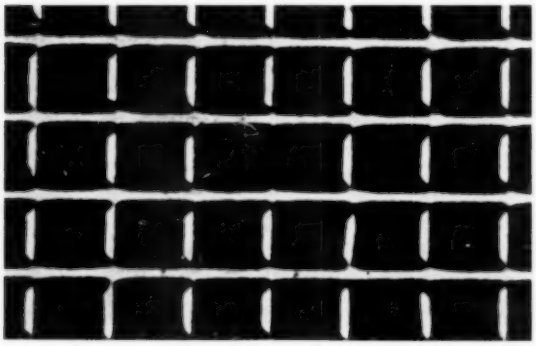

Fig. 1. Microradiogram of a silver grid. The width of each bar is 3 microns; structures as small as 0.5 micron are resolved.

Prof. V. E. Cosslett, Cambridge, England) registered on Eastman Kodak Spectroscopic Plate 649, which was used in this investigation. The bars in the grid are 3 microns in diameter and it is clearly seen that structures smaller than 0.5 micron produce images and the definition is limited by the grain size of the photographic emulsion.

When a microradiogram of a section of bone tissue is registered under controlled conditions, it is possible to interprete the density variations in the image in terms of distribution of mineral salts as is evident from the following reasoning.

The roentgen rays are absorbed in matter according to the expression:

$$E = \ln \frac{I_o}{I} = \frac{\mu}{\varrho} \cdot m \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

where the symbols represent:

E = extinction of roentgen rays $= \ln \frac{I_o}{I}$
I_o = intensity of incident roentgen rays
I = » » transmitted roentgen rays
m = weight of sample in $g \cdot cm^{-2}$
μ = linear absorption coefficient cm^{-1}
ϱ = density of sample $g \cdot cm^{-3}$

The expression $\frac{\mu}{\varrho}$ is the mass absorption coefficient which has the dimension $cm^2 \cdot g^{-1}$.

For bone tissue expression, 1 may be written in the following way, as bone contains one inorganic and one organic fraction,

$$E = \ln \frac{I_o}{I} = \frac{\mu_i}{\varrho_i} \cdot m_i + \frac{\mu_o}{\varrho_o} \cdot m_o \quad \ldots\ldots\ldots\ldots \quad (2)$$

where indices i and o stand for inorganic and 'organic' fractions respectively. The 'organic' fraction may naturally be divided into water and organic substances but in general the ground sections had been preserved in absolute alcohol and their water content was low; no further division of the 'organic' fraction is therefore necessary.

The photographic emulsion does not have a linear density response over a wide exposure range. On exposure of each microradiogram of bone tissue, therefore, a step-wedge made up of aluminium foils was exposed simultaneously. A comparison of the photographic density of a certain bone structure in the microradiogram with the density under the step-wedge, makes it possible to express the roentgen absorption of a certain bone structure in equivalents of Al-absorption *i. e.* in g Al

Fig. 2. Enlargement of microradiogram of a bone section and the reference system with its 11 steps marked 1, 2, 3 etc. Roentgen absorbing structures appear black. One semicircular canal, s. c., is seen. × 15.

per cm^2 or 10^{-12} g Al per square micron (Fig. 2 and Diagram 1). The objection can be raised that when polychromatic roentgen rays are used the wavelength dependence of aluminium is not the same as for bone. If one considers the numerical values of the mass absorption coefficients for protein (represented by nitrogen) and calciumphosphate (apatite), which values are presented in Table 1, it becomes evident that for bone tissue and the wavelengths used the organic contribution to the total roentgen ray absorption may be neglected in comparison with the attenuation caused by the inorganic constituents (ENGSTRÖM, 1946). This is still more evident from the fact that the specific gravity of apatite is about 3 times that of the protein and the attenuation of the roentgen rays is proportional to $\frac{\mu}{\varrho} \cdot m$ where m is the thickness of sample times the specific gravity. Expressed in another way, Formula 2 may be written,

$$E = \ln \frac{I_o}{I} = \frac{\mu}{\varrho} \cdot d \cdot \varrho = \mu \cdot d \quad \ldots\ldots\ldots\ldots\ldots (3)$$

where d is thickness of sample in cm and μ the linear absorption coefficient with the dimension cm^{-1}. It is also seen from Diagram 2 that for the roentgen energies used in our experiments the wavelength dependence of the absorption in Al does not differ greatly from that of the apatite. It is therefore permissable to compare the relative distribution of mineral salts by the technique just outlined above, especially as all samples were exposed with the same energy of roentgen rays.

The fine-grained photographic emulsions are very insensitive, due to the small grain size and the very thin emulsion layer. The emulsions

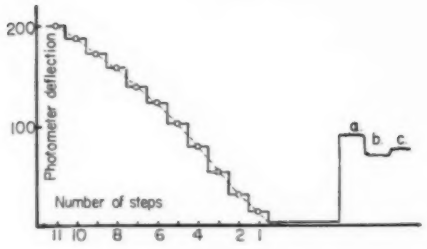

Diagram 1.

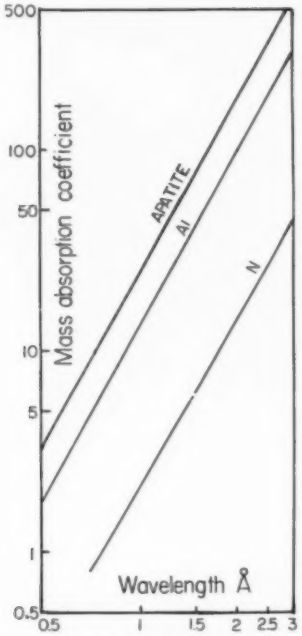

Diagram 2.

Diagram 1. Photometric trace of the reference system and the zone of high mineralization and the less dense neighbouring structure indicated by the letters a, b, and c in Fig. 3 A.

Diagram 2. Mass absorption coefficients for N, Al and Ca as functions of wavelength and plotted to a double logarithmic scale.

Table I

Mass absorption coefficients for apatite and nitrogen

Roentgen energy		Massabsorption coefficient $\frac{\mu}{\rho}$, $cm^2 \cdot g^{-1}$	
kV	Å	Apatite	Nitrogen
24.68	0.5	∾ 3.5	∾ 0.4
12.34	1.0	26	2.1
8.22	1.5	81	7.7
6.17	2.0	178	19
4.94	2.5	330	29
4.11	3.0	545	57

used in these experiments were about 10,000 times less sensitive than ordinary roentgen film, for example, Kodak No Screen roentgen film. When great differences in exposure occur there are certain risks of

development artefacts. White lines (Mackie lines) will appear, especially on the border between heavily and lightly exposed areas. These development artefacts may be minimized by prolonged development and by choosing the sample thickness and roentgen ray wavelengths in such a way that the intensities of the roentgen rays transmitted do not vary to an extreme degree.

Experimental techniques

The experimental equipment consisted of a Machlett OEG 50 roentgen tube which has a 0.2 mm Be window. The focus to film distance was 10 cm and the exposure times varied between 30 seconds and 5 minutes. The microradiograms were developed in Kodak DK 50 developer and further treated according to standard procedures.

The microradiograms were registered with 24 kV and 12 mA and the experimental proof that the original roentgen films really showed the distribution of mineral salts was easily tested by taking a microradiogram after decalcification of the ground section. After such a treatment the contrast in the sample was so low that no roentgen image at all could be obtained. This result of course was expected from the theoretical consideration (cf. Formula 2). As already shown in Fig. 2 and Diagram 1 an aluminium step-wedge was exposed simultaneously with the bone sample. The densities in the original microradiogram were recorded with Zeiss Schnell Photometer II. From these density measurements (Diagram 1) it was possible to express the absorption of the bone tissue in terms of the step-wedge. The relative variations in the concentration of mineral salts were determined only for structures lying quite close to each other, as the sample thickness could be considered constant only within limited areas. As no absolute measurements of thickness were performed, only relative values of the distribution of the mineral salts were obtained. In fact the absolute amounts of mineral salts have very little interest for this investigation.

Results

The microradiograms shown in this communication are photomicrographs of the original microradiograms. In what follows these enlargements will be called microradiograms, the correct term 'photomicrograph of a microradiogram' being unwieldy. A high mineral content in a structure is represented by a white area in the microradiogram. The microradiograms of ground sections of the malleus and incus are shown in Fig. 3. These specimens were taken at an autopsy of a middle-aged woman with no clinical signs of otosclerosis. It is clearly seen from the figure that there is a zone of high mineralization around the caput

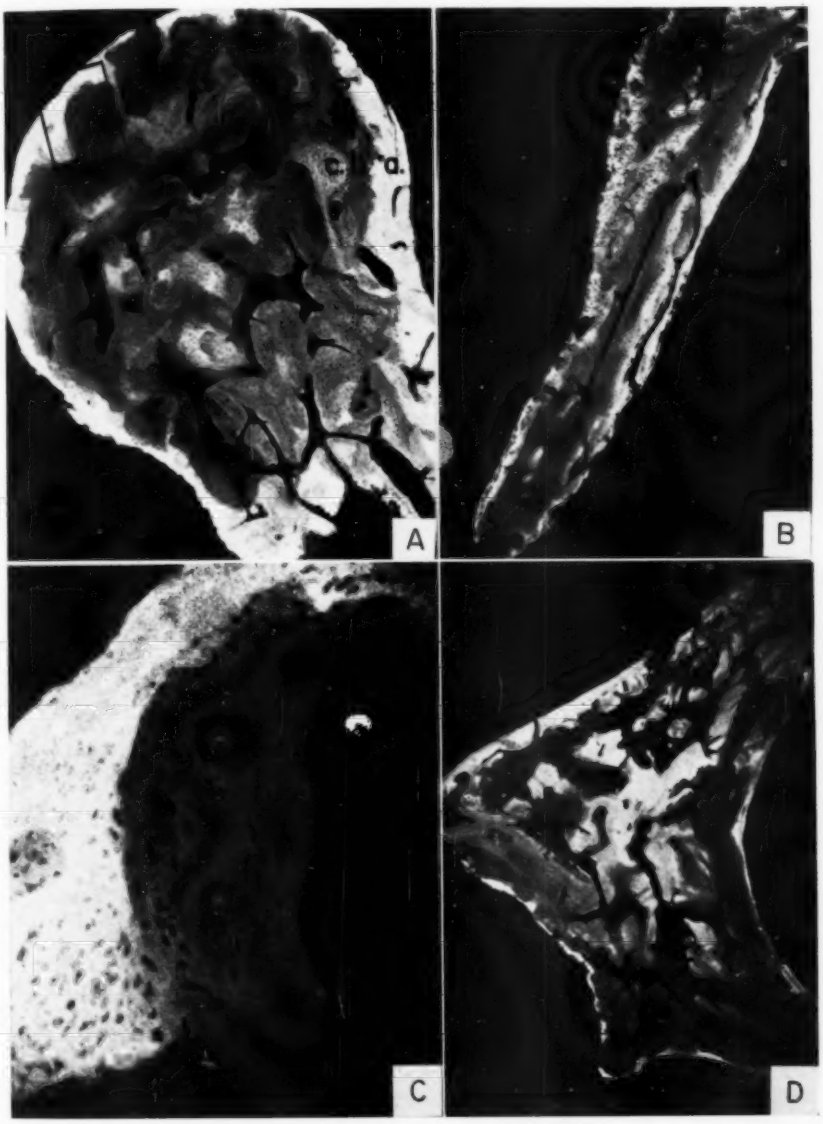

Fig. 3. Microradiograms of malleus and incus. A. Caput mallei, × 70; The points a, b and c refer to Diagram 1. B. Manubrium mallei, × 48, and C. The part of the caput mallei shown in the square in Fig. 3 A, × 318. D. Incus, × 28.

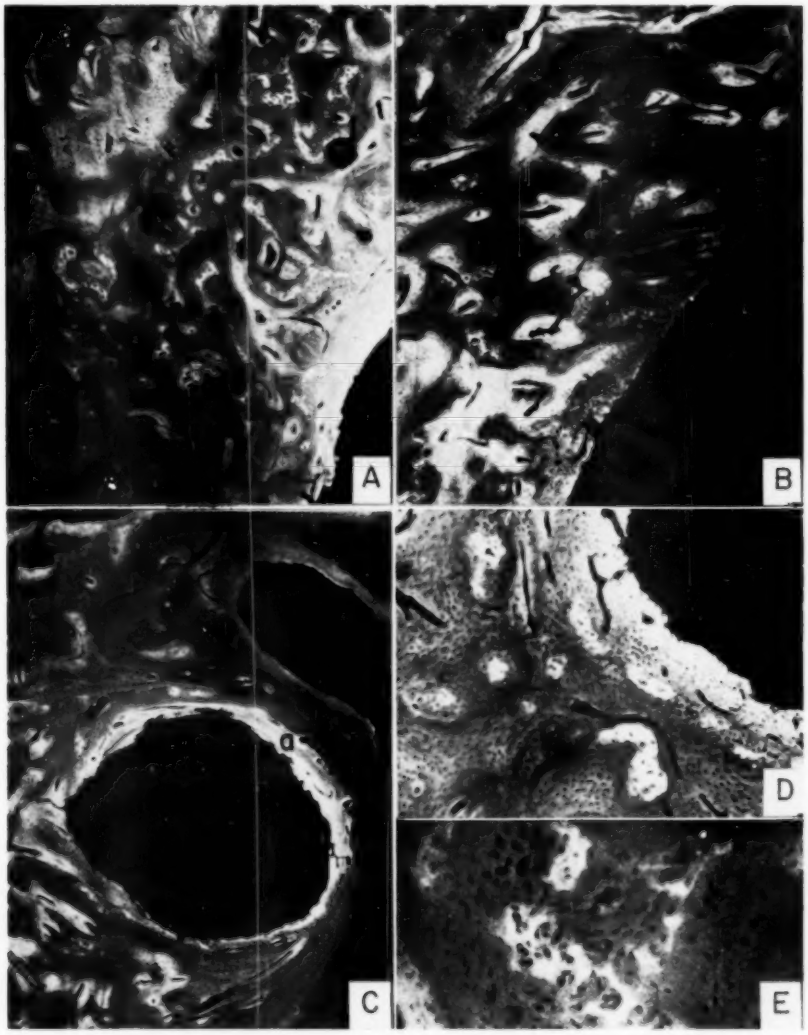

Fig. 4. Microradiograms of the osseus labyrinth. Magnifications: A, × 47; B, × 61; C, × 46; D, × 88 and E, × 218.

mallei. In the centre the formation of the haversian systems may be seen and, like the structure of the diaphysis of the long bones, these are less mineralized than the surrounding bone tissue. In Fig. 3 A two such systems are marked 1 and 2. The square at the left top of Fig. 3 A is shown at a higher magnification in Fig. 3 C. The photometric measurements disclosed that the outer, white zone in Fig. 3 C corresponded to 4.2 steps in the wedge while the inner black area corresponded to 3. This area of the outer zone thus contained about 40 % more mineral salts. The haversian system marked 1 in Fig. 3 A contains 5 to 10 % less mineral salts than the adjacent bone tissue. The haversian system at 2 contains only two-thirds of the mineral content in the neighbouring white zone. Fig. 3 B shows a microradiogram of the manubrium mallei and the vascularization and mineral pattern are well demonstrated. The outer more highly mineralized zone contains 10 to 30 % more mineral salts than the inner less mineralized tissue.

The pattern of mineral distribution in the incus as demonstrated in Fig. 3 D shows essentially the features of Fig. 3 A. The photometry revealed that the outer layer and the central portion had approximately the same mineral content.

Figure 4 shows microradiograms from the osseous labyrinth. There is a peculiar appearance of the bone tissue in Fig. 4 A where recently formed haversian systems (1, 2 and 3) are surrounded by bone tissue in which there are islets of high mineralization. These islets are shown in higher magnification in Fig. 4 E. In Fig. 4 B there is a type of mineralization which is not found in the long bones. The high content of mineral salts around the blood vessels is the most outstanding feature. Mineralization is high around a semicircular canal as shown in Fig. 4 C and at a higher magnification in Fig. 4 D. At points a and b in Fig. 4 C the absorption is equivalent to 4.6 and 2.8 steps in the Al-wedge respectively which means about 65 % more mineral salts at a.

In this investigation bone tissue from only a few cases of adults has been investigated. A systematic study of the distribution of the mineral salts in the auditory ossicles of varying age may reveal significant changes in the pattern of mineral salt distribution. As in this investigation only a few cases have been examined, no general conclusions can be drawn. It seems, however, that it may prove possible to describe the pattern of the distribution of the mineral salts and its change with age by a comparative study of a large material in which all ages are represented. Such an extensive material will form the basis for further investigations, now planned, of otosclerotic processes.

In addition to the human material some microradiograms of the osseous labyrinth of the rabbit were registered. The findings were in essential the same as in the former material.

SUMMARY

A simplified theory for the microradiographic demonstration of the distribution of mineral salts in thin bone sections is first presented. The experimental technique is described in detail. Microradiographic examination of thin ground sections from the malleus, incus and osseous labyrinth revealed a characteristic mineral pattern, the significance of which is discussed.

ZUSAMMENFASSUNG

Eine vereinfachte Theorie für die mikroradiographische Demonstration von Mineralsalzen in dünnen Knochenschnitten wird anfangs vorgelegt. Die experimentelle Technik wird ausführlich beschrieben. Die mikroradiographische Untersuchung dünner Gewebsschnitte vom Malleus, Incus und dem knöchernen Labyrinth zeigten ein charakteristisches Mineralmuster, dessen Bedeutung diskutiert wird.

RÉSUMÉ

Les auteurs présentent d'abord une théorie simplifiée pour la mise en évidence microradiographique de la distribution des sels minéraux dans des coupes osseuses minces. La technique expérimentale est décrite en détail. L'examen microradiographique de coupes par abrasion minces du marteau, de l'enclume et du labyrinthe osseux ont révélé une disposition minérale caractéristique dont les auteurs étudient la signification.

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FROM THE DEPARTMENT OF GYNAECOLOGY (DIRECTOR: PROF. P. WETTERDAL), SABBATSBERGS SJUKHUS, KAROLINSKA INSTITUTET, STOCKHOLM, SWEDEN

ACTIVATION ANALYSIS WITH A POLONIUM^{210} ALPHA SOURCE

by

Erik Odeblad

Activation analysis has been applied to biologic and medical problems in a number of published investigations. Pile neutrons (TOBIAS and DUNN, 1949, TOBIAS, WOLFE, DUNN and ROSENFELD, 1952) or cyclotron beams (ODEBLAD and TOBIAS, 1954) have been utilized. It has also been found that activation occurs in cells irradiated with high energy roentgen rays (BALDWIN and CLARK, 1953) or high energy deuteron beams (TOBIAS, VAN DYKE, SIMPSON, ANGER, HUFF and KONEFF, 1953). Other papers on activation analysis in biology have also appeared.

The performance of activation analysis using simpler sources of irradiation than piles and particle accelerators have been searched for. MEINKE and ANDERSON (1953) described a 25 mg radium-beryllium neutron source for low-level activation analysis.

In the present paper the principles underlying the use of a polonium^{210} source for activation with alpha particles are described. The applications of the polonium^{210} alpha source to specific biologic problems and in autoradiography are now proceeding and will be reported in due course.

Theoretical aspects

If a sample containing target nuclei, T, is irradiated with alpha particles of low energy, as in the present experiments, the nuclear reaction apparently proceeds over an excited compound nucleus, J, which can be de-excitated in several competing ways. The reaction products are a final nucleus, R, and a particle, r. We can write:

$$T + a \rightarrow J \rightarrow R + r + Q.$$

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Here Q expresses the energy balance of the reaction. If Q is negative, the reaction is energy-consuming (endothermic), if Q is positive, it is exothermic.

If R is a radionuclide, it can be easily detected. The sample is 'activated' and analytical procedures of T can be based on that particular nuclear reaction, *i. e.* activation analysis can be performed.

If alpha particles are used for the nuclear bombardment, the formation of the compound nucleus J is often markedly restricted by the potential barrier surrounding the target nucleus. The probability of penetration is expressed by the Gamow factor, which varies between 0 and 1. In cases of resonance penetration, the probability is higher than given by the Gamow factor. The existence of the potential barrier implies that the penetration of polonium^{210} alphas is negligible if the atomic number is higher than about 20.

Not only the conservation of energy and the Gamow factor limit the possible nuclear reactions with the polonium alphas. The conservation of angular momentum and charge in any particular nuclear reaction highly restrict the permitted reactions. In the practical performance of activation analysis it is also important that the half-life of the radionucleide formed is not too short or too long. The properties of some energetically permitted nuclear transformations yielding radionuclides of appropriate half-lives are summarized in table I, together with some experimental results.

Experimental

The polonium source. The source of alpha radiation (manufactured by A. E. R. E., Harwell, England) consisted of (originally) 160 mC of uncovered polonium^{210}, electroplated within a circular area, 1 cm in diameter, on a circular platinum disc, 2 cm in diameter. Since Po^{210} emits practically only alpha rays (10^{-3} per cent gamma rays) the shielding is no difficult problem. On the other hand, the high internal toxicity of polonium^{210} implies that extreme care must be taken to avoid contamination. The flux of the 5.3 MeV alpha rays, $3.0 \cdot 10^9$ per sec., from the source, corresponds to an undirected current of about 10^{-3} μA hitting the target.

Fig. 1. Pinhole autoradiograph (about 1 : 1) of the polonium source, showing some inhomogeneity in the distribution of polonium within the radiating area. White areas indicate polonium.

The Po^{210} source was estimated to have a mean thickness of about 80 $\mu g/cm^2$, thus giving a negligible self-absorption of alpha rays. The uniformity of the source was investigated with a pinhole camera. A pinhole autoradiograph is shown in fig. 1.

The technique of irradiation. When powdered samples were used, they were placed in small lead discs since lead gives no detectable nuclear interaction with Po^{210} alphas. The upper surface of the powdered sample was pressed so that it should have a smooth surface. If metallic foils were irradiated, layers of oxide, sulfide etc. on the surface were removed. Histologic sections were irradiated after mounting on methacrylate slides, or lead. The distance between the source and the target was about 0.5 mm of air of normal temperature and pressure, reducing the energy of the alphas by about 0.1 MeV or less before entering the target. After finishing the bombardment the sample was introduced into the Geiger-Müller counter as rapid as possible.

The alpha particle energy is finally more or less dissipated as heat in the target. If only this process occurred, the target would receive 0.035 cal./min.

Technique of counting. When the half-life of the radionuclide exceeded about 2 minutes, it was as a rule possible to operate the counter manually. More short-lived activities were visualized as Geiger-Müller impulses on a cathode ray oscillograph screen and recorded photographically on moving film.

The counter usually used had a cylindrical tube. The geometry was so arranged that $1.44 \cdot 10^{-5}$ mC U^{234} gave rise to 74 ± 1 counts per sec., corresponding to 14 per cent space efficiency.

Results

1. Activation of chemical compounds and elements. The theoretical basis and the results are given in table I. The theoretical figures are based upon a large number of references given by BAINBRIDGE (1953) and BEYER (1949).

Carbon, *oxygen* and *hydrogen* were examined as graphite, paraffin, methyl methacrylate and glucose. No detectable activity was found after alpha irradiation by the Po^{210} source, as predicted by theory.

Nitrogen. Nitrogen was examined as $(NH_2)_2CO$ and $(NH_4)_4SO_2$. The energetically permitted reaction $N^{14}(\alpha,\gamma)F^{18}$ gave a hardly detectable yield. This is so weak, that no practical analysis of nitrogen can be based on it.

Boron. Irradiated H_3BO_3 and $Na_2B_4O_7$ showed a 10.0 ± 0.2 minute activity, identified as N^{13}. The yield is high enough to permit the analysis

Table I

Energetically permitted nuclear reactions in light elements with polonium alphas, giving radionuclides of half-lives between 3 sec. and 3 years

I	II	III	IV	V	VI	VII
$B^{10}(a, n)N^{13}$	10.1 min.	+ 1.1	H_3BO_3	26	1.4	10^{-8}
$N^{14}(a, \gamma)F^{18}$	1.9 hr	+ 4.4	$(NH_2)_2CO$	1	10^{-3}	10^{-1}
$F^{19}(a, n)Na^{22}$	2.6 year	— 2	LiF	0.5	2.2	10^{-4}
$Na^{23}(a, n)Al^{26}$	6.5 sec.	— 3	NaCl	38	0.2	10^{-3}
$Mg^{25}(a, p)Al^{28}$	2.3 min.	— 1.2	Mg	52	1.2	10^{-8}
$Al^{27}(a, n)P^{30}$	2.5 min.	— 2.9	Al	320	0.8	10^{-4}
$K^{39}(a, \gamma)Sc^{43}$	4.0 hr	+ 4	KCl	4	$^1 10^{-2}$	10^{-1}
$K^{41}(a, n)Sc^{44}$	4.0 hr	— 3	KCl		$^1 10^{-1}$	
$Ca^{40}(a, \gamma)Ti^{44}$	2.7 year	? + 5	CaO	—	—	—
$Ca^{40}(a, p)Sc^{43}$	4.0 hr	— 4	CaO	—	—	—

Columns: I: Nuclear reaction. II: Half-life of induced radioactivity. III: Q-value of the reaction in MeV. IV: Irradiated substance, upon which the values in the following columns are founded. V: Experimental initial yield in counts per sec. at saturation (except for the radionuclides Na^{22} and Ti^{44} where 48 hours irradiation was used). VI: Isotopic yield of the reaction: nuclear transformations per 10^6 alphas from polonium-210 in a hypothetically pure isotope sample. VII: Order or size of the least measurable quantity of irradiated element with an error of ten per cent, in grams.

[1] The yields given for the two potassium isotopes are maximum values if only one of the reactions is operating.

of boron. It is the isotope B^{10} which gives rise to N^{13}. B^{10} is present to the extent of about 19 per cent in natural boron. If boron is determined in some other way, B^{10}, enriched and used as a tracer could be determined with alpha activation.

Fluorine. The reaction $F^{19}(a,n)Na^{22}$ has been detected in LiF and NaF. The very long half-life of Na^{22} requires long irradiation times (48 hours and more) if detectable amounts of Na^{22} are to be formed. The long half-life demands long counting times to obtain statistically certain results, and the yield is good enough to permit fluorine analysis.

Sodium. Irradiation of $NaNO_2$, NaCl and NaF gave rise to a fairly good activity of 6.5 ± 0.5 sec. half-life, Al^{26}. The yield is good enough to permit the quantitative analysis of Na. The short half-life is a complication and repeated activations are required to obtain statistically certain results.

Magnesium. Irradiated magnesium as metal, MgO and $MgCl_2$ exhibits a 2.2 ± 0.1 min. activity of Al^{28} with a good yield. This permits the quantitative analysis of Mg. The reaction giving Al^{28} proceeds from the nuclei Mg^{25}, forming about 10 per cent of natural Mg. If Mg is determined in some other way, activation with alphas can be used to determine enriched Mg^{25} used as a tracer.

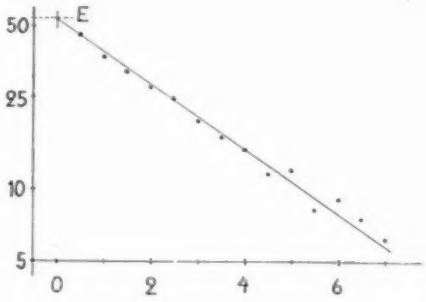

Diagram 1. Decay curve of irradiated pure magnesium. Ordinate: counts per second, logarithmic scale. Abscissa: time in minutes after finishing activation. E is the extrapolated activity at time zero. The activation lasted 15 minutes.

Aluminium. Bombarded Al, $AlCl_3$ and $Al(NO_3)_3$ gave a 2.4 ± 0.1 activity of P^{30} in very good yield, enabling the quantitative analysis of Al.

Phosphorus, sulfur and *chlorine* gave no detectable radioactive products as predicted by the theoretical Q-values.

Potassium. In irradiated KCl, KBr and K_2CO_3 a 3 ± 1 hr radioactivity was found in very small yield. Though the reaction products can be formed in two ways, the yield is too weak to permit the quantitative determination of potassium. It is uncertain which of the two ways dominates here. In performing countings on potassium compounds, allowance must be made for the natural radioactivity of potassium (K^{40}).

Calcium. Irradiated CaO and $CaCl_2$ gave no detectable yield.

Higher elements. Attempts to detect the reactions $Co^{59}(\alpha, n)Cu^{62}$, $Ni^{60}(\alpha, n)Zn^{63}$, $Ag^{107}(\alpha, \alpha')Ag^{107m}$ and $Ag^{109}(\alpha, \alpha')Ag^{109m}$ failed.

Table II

Determination of Na^{23} in urine ash.

	Integrated counts 5 to 35 seconds after activation of	
	urine ash	sodium chloride
	16	185
	25	189
	24	210
	18	202
	28	236
	15	224
	22	226
	23	188
	27	198
	21	209
Mean	22 ± 2	207 ± 28

2. Biologic applications. The reaction $Na^{23}(\alpha, n)Al^{26}$ has been detected in ash from *blood serum*, *urine* and *liver*. In urinary specimens Na has been evaluated in the following way. Wet urine ash was prepared and irradiated for 1 min. with Po^{210} alphas. The integrated count over the period 5 to 35 sec. after irradiation was recorded. The same was done for NaCl. The results are shown in table II, indicating that about 11 ± 3 per cent of NaCl activity was found in urine ash. A more careful study in this field is proceeding and will be reported later.

In rats $KAl(SO_4)_2$ was introduced intraperitoneally in a 1 per cent solution and repeated specimens were taken up to two hours after injection. Determination of Al with activation analysis showed no decrease of the Al concentration during this period of time.

Discussion

The present study clearly indicates that it is possible to activate and determine the stable isotopes B^{10}, F^{19}, Na^{23}, Mg^{25} and Al^{27}. Activation has been undertaken both in pure chemical preparations and in biologic samples.

Since the range of Po^{210} alphas, even in materials of low stopping power is less than 15 mg/cm², there is no need for thick samples in carrying out activation of the kind described here. Fifteen mg is a sufficient quantity, provided it can be prepared as a thin even layer. At present it has been possible to determine the amounts of elements as indicated in the last column in table I. These amounts do not seem encouraging, especially when compared with the results of pile neutron activation analysis, in which 10^{-9} grams can be determined of many elements. However, the analytical procedure here is very simple and very rapid excepting in the case of fluorine, where it takes long time.

One advantage of the method described is that the sample is not destroyed by the analytical process, which can be repeated many times without damage. Another advantage is that the radioactivity induced is weak enough not to require any shielding; this lightens the work. Finally it can easily be performed in any radioisotope laboratory.

The main disadvantages are the limited number of isotopes it is possible to activate and the relatively low sensitivity of the method.

SUMMARY

A 160 mC Po^{210} source was used for alpha particle activation of pure chemical compounds and biologic material. The stable isotopes it was found possible to activate to radionuclides in any appreciable extent were B^{10}, F^{19}, Na^{23}, Mg^{25} and Al^{27}, giving N^{13}, Na^{22}, Al^{26}, Al^{28} and P^{30} respectively. The isotopic yields were between 0.2 and 2.2 per 10^6 alphas. Two biologic applications were studied: the measurement of sodium in urine and the resorption of aluminium from the peritoneal cavity.

ZUSAMMENFASSUNG

Die Alfa-partikeln einer Strahlenquelle von 160 mC Po^{210} wurden für Aktivierung von reinen chemischen Substansen und biologischen Objekten verwendet. Die stabilen Isotopen B^{10}, F^{19}, Na^{23}, Mg^{25} und Al ^{27} könnten mit genügenden Resultat aktiviert werden und gaben die Radioisotopen N^{13}, Na^{22}, Al^{26}, Al^{28} und P^{30}. Die isotopische Transmutationsfrequenz war zwischen 0.2 und 2.2 pro 10^6 Alfa-partikeln. Von biologischen Probleme wurden die Bestimmung von Natrium im Harn und die Resorption von Aluminium aus die Peritonealhöhle studiert.

RÉSUMÉ

Des particules alfaémises par une source de rayons consistant en 160 mC de Po^{210} ont été employées pour activer des substances chimiques pures et des préparations biologiques. On a réussi à activer, de façon satisfaisante, les isotopes B^{10}, F^{19}, Na^{23}, Mg^{25} et Al^{27} en radio-isotopes N^{13}, Na^{22}, Al^{26}, Al^{28} et P^{30}. Le nombre des transmutations nucléaires a été pour ces réactions de 0.2 à 2.2 par 10^6 particules alfa. Parmi les applications biologiques on a étudié la détermination de Na dans les urines ainsi que la résorption de Al de la cavité péritonéale.

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FROM THE INSTITUTE OF RADIOPHYSICS (DIRECTOR: PROFESSOR ROLF M. SIEVERT), KING GUSTAF V JUBILEE CLINIC, STOCKHOLM, SWEDEN

ROENTGEN DOSE MEASUREMENTS ON A RADIATION OF VERY HIGH INTENSITY

by

Bo Lindell

During experiments with a discharge roentgen tube, giving single dose pulses of short duration and very high intensity (SIEVERT (9); LINDELL, SIEVERT & WAHLBERG (5)) it was necessary to know the reliability of the measured dose values. For that reason the performance of some thimble chambers was investigated, with the result that the lack of saturation, depending upon the recombination of ions, was found to be in good agreement with the values which could be predicted by theory, even when the intensity was extremely high (giving dose-rates up to 10^7 r/sec).

Dose measurements and the determination of saturation curves

All dose measurements were made inside a cylindrical anode, constructed as a transmission target and designed for irradiation of small biologic objects such as Drosophila eggs and mice (cf. Fig. 1).

In a volume, 3 cm in diameter and 7 cm high, roentgen doses up to 1,000 r per discharge were measured, the corresponding irradiation time being shorter than 100 microseconds. In this volume the dose at any single discharge varied less than 10 per cent along the central axis and less than 5 per cent in the radial direction. The standard deviation of the measured dose in a particular point at different discharges with the same high voltage was about 10 per cent, this giving an idea of the reproducability.

The examined chambers were of two kinds. Most convenient for the high doses inside the anode cylinder were the small SIEVERT condenser chambers (8) developed for measurements of therapy doses, having a

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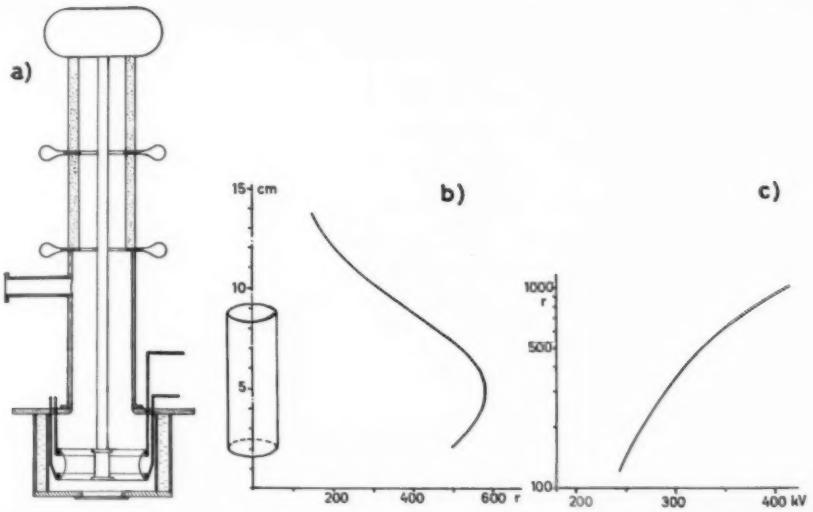

Fig. 1. a) Section of discharge tube showing the cylindrical anode surrounded by filaments.
b) Dose distribution along the axis of the anode in the region in which biologic specimens are placed for irradiation.
c) Maximum dose as a function of condensor voltage.

measuring range up to 600 r. Dr. R. THORÆUS of this institute has recently designed a longer type of this chamber, capable of measuring up to 1,000 r, due to the increased capacitance. He kindly put at my disposal a copy of it, which closely covered the demand on sensitivity in the dose measurements in the biologic experiments with the discharge tube.

Chambers of these types have proved to be widely independent of wavelength. The accurately known dimensions of the ionized volume make it possible to compare theoretical estimations and experimental investigations as to the degree of saturation at the extremely high dose-rate and short exposure time used in the experiments, and accordingly to study the corrections required. This is also of general interest as similar chambers may be used in the future to measure therapy doses at high intensities, for example from betatrons or linear accelerators, and it should be valuable to know as much as possible about their performance in high intensity radiation.

For protection measurements outside the discharge tube cardboard double chambers were used (SIEVERT & WALSTAM (10)).

The degree of saturation in both these types of chamber was measured in the following way. Each chamber to be examined was irradiated

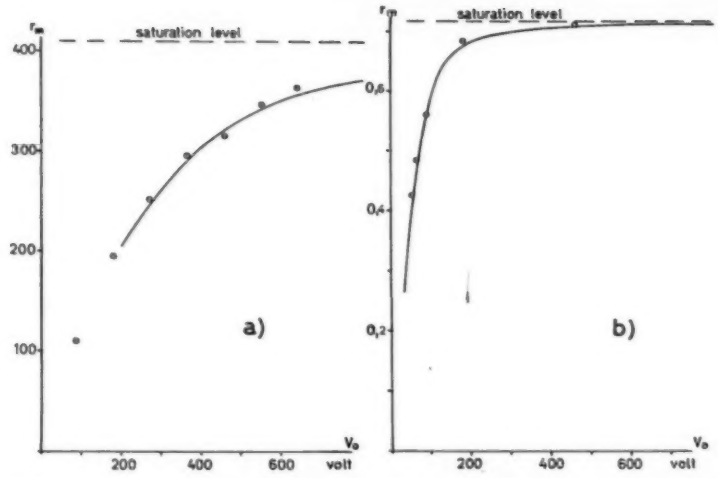

Fig. 2. Saturation curves for a) 1,000-r-chamber b) double chamber. Points indicate measured values and curves the theoretical relation between measured dose and chamber voltage.

with one and the same dose at different chamber voltages. As the reproducability of the discharge tube during these experiments was bad, the dose could not be expected to be constant throughout a series of measurements. For that reason another chamber, charged to a fixed voltage, was irradiated at the same time as the one tested. The reading on this control chamber made it possible to make a correction for dose variations, enabling all measurements to be referred to the same dose value within the accuracy of the chambers. Examples of the resulting saturation curves are shown in Fig. 2.

Theoretical interpretation of the saturation curves

In the theoretical estimation of the ionization loss caused by recombination of ions one has to consider that one of two principally different conditions may be fulfilled, viz.

A. The time required for ion collection is much longer than the duration of the ionizing pulse. The dose may be considered to be delivered instantaneously, since the ion drift during the irradiation may be neglected. Only the total ionization, *i. e.* the dose per pulse, will affect the result.

B. The collection time is much shorter than the duration of the irradiation pulse. Then the time required to build up an equilibrium may

be neglected and the chamber regarded as working under equilibrium conditions through the major part of the pulse.

In this section the following symbols will be used:

a = inner radius in cylindrical or spherical chambers (cm).
α = recombination coefficient (for air $\approx 1.6 \times 10^{-6}$).
b = outer radius corresponding to a.
β = constant defined by Eq. 9.
d = electrode distance (cm).
e = I/i.
ε = relative ionization loss due to recombination = $1 - i/I$.
$\bar{\varepsilon}$ = mean value of ε for a condensor chamber.
γ = constant defined by Eq. 3.
i = ionization current.
I = saturation current.
j = mean dose-rate = r/τ.
k = chamber constant (volt/r).
n_0 = instantaneous ionization, number of ion pairs per cm^3.
q = number of ion pairs produced pr cm^3 and second.
r = r_0 = roentgen dose per pulse.
r_m = measured dose value = $(1 - \bar{\varepsilon}) \times r_0$.
T = time required for collection of ions (sec).
τ = pulse duration or irradiation time (sec).
u = ion mobility ($u^+ + u^- \approx 3.1$ cm/sec per volt/cm).
V = chamber voltage (V_0 original voltage, V_r remaining voltage after irradiation).

The time that is required for ion collection may be estimated from

$$T \approx \frac{d^2}{(u^+ + u^-)V} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

In the present investigation, although the duration of the pulses was less than 100 microseconds, the conditions presumed in case A did not seem to be valid since the chambers employed had rather short electrode distances

	d cm	V_0 volt	T μs
1,000-r-chamber	$\geqq 0.07$	700	2
double chamber (inner part)	0.12	90	50

At least the therapy chamber must be considered to have worked under equilibrium conditions, but as the pulse duration was estimated with great uncertainty it was not possible to say at once whether the double chamber also may have had an equilibrium, or if it should be treated according to some compromise between the cases A and B.

Case A. Negligible pulse time.

This case has been treated by LANGEVIN (4), who has given a formula for the ionization loss caused by recombination. According to BOAG

(1), (2) his formula can be applied to the dose measurements on roentgen pulses of very high dose-rate and short duration, *e. g.* the radiation from linear accelerators and impulse generators with a pulse duration of the order of one microsecond. Then

$$\varepsilon = 1 - \frac{1}{z} \cdot \ln\,(1 + z) \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (2)$$

In the one-dimensional case (parallel plate-chamber) we have

$$z_p = \frac{a n_0 d^2}{(u^+ + u^-)V} = \gamma \times \frac{r}{V} \quad \ldots\ldots\ldots\ldots\ldots \quad (3)$$

Eq. 2 is also valid for a cylindrical chamber (cf Boag (1]) if z_p is replaced by z_c where

$$z_c = \left[\frac{b + a}{b - a} \times \frac{\ln \frac{b}{a}}{z}\right] \times z_p = f_c \times z_p \quad \ldots\ldots\ldots\ldots \quad (4)$$

and for a spherical chamber, with

$$z_s = \frac{1}{3}\left[\frac{b}{a} + 1 + \frac{a}{b}\right] \times z_p = f_s \times z_p \quad \ldots\ldots\ldots\ldots \quad (5)$$

f_c and f_s do not differ very much from unity for any chamber not constructed for proportional counting purposes. As the uncertainty in the constant γ is rather high we may write

$$z = \text{const} \times \frac{r d^2}{V} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (6)$$

valid for any of the chamber shapes mentioned above. The constant should then be determined empirically in each particular case. In air (NTP) for a parallel plate-chamber it is approximately 1,000.

For small values of ε the relative recombination loss may be taken from

$$\varepsilon = \frac{z}{2} \approx 500 \times \frac{r d^2}{V} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (7)$$

Case B. Negligible time for collection of the ions.

The performance of an ionization chamber at equilibrium conditions is well known and the relative recombination loss is easily estimated (cf Appendix). Approximately it can be written as

$$\varepsilon = 1 + x - \sqrt{x\,(2 + x)} \quad \ldots\ldots\ldots\ldots\ldots \quad (8)$$

where for a parallel plate-chamber (or a cylindrical chamber with not too small value of a/b)

$$x = \frac{3}{4}\frac{(u^+ + u^-)^2 V^2}{\alpha q d^4} = \beta \times \frac{V^2}{j} \quad \ldots\ldots\ldots\ldots\ldots (9)$$

in air $\beta \approx 0.0022/d^4$, and for small values of ε

$$\varepsilon = \frac{1}{2x} = \frac{1}{2\beta} \times \frac{j}{V^2} \quad \ldots\ldots\ldots\ldots\ldots\ldots (10)$$

For cylindrical chambers SEELIGER (7) has given the formula

$$V = C\frac{\sqrt{q}}{\sqrt{\varepsilon}\sqrt{e-1}}a^2\left(\frac{b^2}{a^2}-1\right)\left\{\left[1 + A\left(\frac{1}{\frac{b^2}{a^2}-1} + \frac{u_\pm}{u_+ + u_-}\right)^2\right]\ln\frac{b}{a} - A\left(\frac{1}{\frac{b^2}{a^2}-1} + \frac{+u_\pm}{u_+ + u_-}\right) + \frac{A}{4}\frac{b^2+a^2}{b^2-a^2}\right\} \quad \ldots\ldots\ldots\ldots\ldots\ldots (11)$$

Seeliger gave for C the value $\sqrt{\alpha}/2(u^+ + u^-)$ and for A in air the value 7.426. For small values of ε the terms containing $(e - 1)$ as a factor may be neglected and the formula be written

$$V = C\frac{\sqrt{q}}{\sqrt{\varepsilon}}2(b-a)^2 \times \left(\frac{b+a}{b-a}\frac{\ln\frac{b}{a}}{2}\right) = 2Cd^2\frac{\sqrt{q}}{\sqrt{\varepsilon}} \times f_c \quad \ldots\ldots\ldots\ldots (12)$$

For a parallel plate-chamber $f_c = 1$ and the equation should be identical with Eq. 10, which gives $C = \sqrt{\alpha}/\sqrt{6}(u^+ + u^-)$ instead of SEELIGER's value. For a cylindrical chamber β in Eq. 9 should be corrected by the factor $1/f_c^2$.

The performance of condenser chambers

All formulae given above deal with the relative ionization loss caused by recombination as a function of the roentgen dose or dose-rate at a given chamber voltage *that has been assumed constant*. Usually, however, the chamber is discharged by the irradiation to such a high degree that the remaining voltage becomes much lower than the original voltage. This results in a greater recombination than can be calculated from the original voltage only.

BOAG (1) gives the following formula, from which the mean recombination and the total charge loss after an *instantaneous* ionizing pulse may be calculated (*Case A*)

$$\bar{\varepsilon} = 1 - \frac{e^{\xi_1}}{z} [-\mathrm{Ei}(-\xi_1) + \mathrm{Ei}(-\xi_2)] \quad \ldots\ldots\ldots\ldots \quad (13)$$

Ei($-\xi$) being the exponential integral, tabulated in *e. g.* JAHNKE-EMDE (Tafel höherer Funktionen, Leipzig 1948). If p is the ratio V_r/V_0 between the remaining voltage and the original voltage on the chamber and T the collection time according to Eq. 1, ξ_1 and ξ_2 mean

$$\xi_1 = \frac{1-p}{2z}, \quad \xi_2 = \frac{1-p}{2z}(1 + an_0T)$$

BOAG points out that there is surprisingly little difference between the mean recombination for $V_r = 0$ and $V_r = V_0$.

In the case of negligible ion collection time (*Case B*), the mean value of ε may be written (cf. Appendix)

$$\bar{\varepsilon} \approx \sqrt{\varepsilon_0 \varepsilon_r} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (14)$$

where ε_0 corresponds to the original chamber voltage V_0 and ε_r to the rest voltage after irradiation. Of course, one cannot say immediately what the rest voltage will be, but as a first approximation it may be taken as $V_1 = V_0 - k(1 - \varepsilon_0)r_0$, k being the chamber constant and r_0 the real dose to be measured. As V_1 will be smaller than the real rest voltage V_r, $\bar{\varepsilon}_1 = \sqrt{\varepsilon_0 \varepsilon_1}$ will be too great. The next approximation $\bar{\varepsilon}_2 = \sqrt{\varepsilon_0 \varepsilon_2}$ (where ε_2 has to be taken for $V_2 = V_0 - k(1 - \bar{\varepsilon}_1)r_0$) will give a too small value and so on, but after a few calculations, the values will have converged to a proper figure that can be used for $\bar{\varepsilon}$ (cf. Fig. 3).

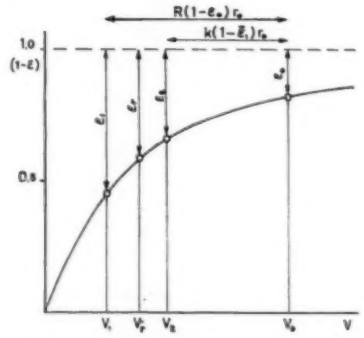

Fig. 3. Estimation of the mean recombination.

Calculation of the saturation level and the real dose

As a result of the dose measurements we have dose values r_m measured at different charging voltages V_0 below the saturation level. For calculation of the real dose r_0 it is necessary to extrapolate these values to saturation voltages using one of the formulae described above.

Case A.

If we trust Eq. 2 putting $1 - \varepsilon_0 \approx 1 - \bar{\varepsilon} = r_m/r_0$ and $z = \gamma r_0/V_0$, r_0 may easily be solved as

$$r_0 = \frac{V_0}{\gamma}\left[e^{\frac{\gamma}{V_0} r_m} - 1\right] \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (15)$$

If, using this formula, we calculate r_0 we find values that differ very much for each of our values of r_m. Hence Eq. 2 is not valid in our case, and the next step is to try Case B.

Case B.

If we use Eq. 8 and, replacing $1 - \varepsilon$ by r_m/r_0, put $x = \beta \frac{V_0 V_r}{j}$ we find

$$r_m = r_0\left[\sqrt{\frac{\beta}{j} V_0 V_r \left(2 + \frac{\beta}{j} V_0 V_r\right)} - \frac{\beta}{j} V_0 V_r\right] \quad \ldots\ldots\ldots \quad (16)$$

The value of r_m is ambiguous, as it may be produced by any value of $r_0 \geqq r_m$ provided that the dose-rate j is arbitrary, *i. e.* we have to know the dose-rate before we can calculate r_0, which may be solved as

$$r_0 = \frac{r_m}{2}\left\{1 + \sqrt{1 + \frac{2\, j/\beta}{V_0 V_r}}\right\} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (17)$$

There is no reason to evaluate the constant β as long as the mean dose-rate is not known accurately. For a given series of measurements j/β may be determined by calculating r_0 for each value of r_m with arbitrarily choosen values of j/β as parameter. If then the spread δ of the calculated r_0-values is plotted as a function of j/β, a distinct minimum of δ gives the value of j/β that makes the experimental values satisfy Eq. 8 in the best way. Of course the right value of j/β should give the same value of r_0 within the limits of normal errors for any value of r_m so far as Eq. 17 is valid. Curves for two different chamber types are shown in Fig. 4, where δ is taken for the four most reliable r_m-values (*i. e.* at the highest charging voltages).

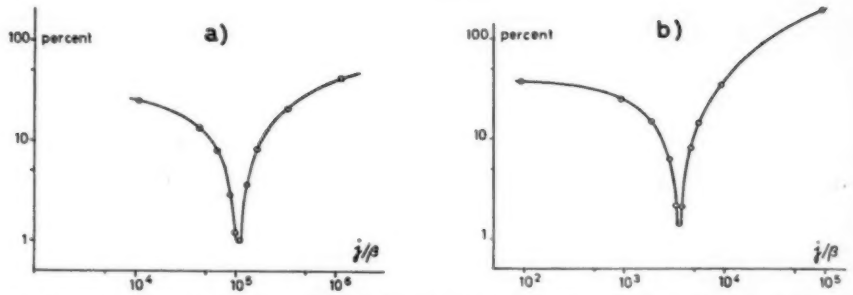

Fig. 4. Curves showing the spread of the calculated r_0-values to give the most proper value of j/β. a) 1,000-r-chamber b) double chamber.

If we take the j/β-value of the minimum as the most proper one, we can calculate the saturation curves from Eq. 16. The result is shown in Fig. 2 where the curves represent these calculations, while the points give the measured doses.

If the irradiation time that corresponds to the mean dose-rate j is calculated, we find values definitely higher than those expected from direct measurements. It seems likely that this discrepancy is due to the fact that part of the charge is transferred by free electrons and not by negative ions. It should be noticed that the formulae given above are meant to be used with the empirical value of j/β obtained as described, irrespective of the actual value of a and u. Concerning the performance of ionization chambers in the case of conduction by electrons and positive ions, the reader is referred to the paper by Boag and Wilson (3).

A two-chamber method for dose measurements at unknown dose-rates

In the preceding section it has been shown that the formula (8), which was derived under conditions valid for long irradiation times and moderate dose-rates (as usual in common roentgen dose measurements), holds true also at very high intensities and short times, provided only that the irradiation time is not shorter than the time required for ion collection.

Even if the dose-rate is not known, it is still possible to determine the recombination and the real dose with the method described above. It is, however, not necessary to make a whole series of measurements; two values of r_m are in fact sufficient to eliminate the unknown ratio j/β in Eq. 17.

If we make a similtaneous measurement with two identical chambers (a and b) charged to different voltages, we can calculate r_0 as

$$r_0 = r_{ma} \frac{\varrho - s}{\varrho - s^2} \quad \ldots\ldots\ldots\ldots\ldots\ldots (19)$$

where $\varrho = (V_0 V_r)_a/(V_0 V_r)_b$ and $s = r_{ma}/r_{mb}$. Thus we are able to express r_0 in the measured values r_m, V_0 and V_r only, and do not need to know the dose-rate, irradiation time (provided that it is sufficiently longer than the time for ion collection; if not, Boag's formula in the shape of Eq. 15 will give the same value of r_0 for both the chambers), recombination coefficient, ion mobility or chamber geometry and dimensions.

In the case in which no recombination takes place, the two chambers should give the same dose value. If not, Eq. 19, which represents an extrapolation instead of an interpolation (for the average) certainly introduces an error instead of reducing it, but for good chambers this error is always negligible.

Influence of varying dose-rate

It may seem surprising that the calculations so accurately describe the experiments, although the dose-rate has in all formulae been assumed to be constant, which is a rough approximation. In our case, however, the ionizing pulse does not seem to have any peak of such short duration that it would modify the presumed equilibrium conditions. In the way the mean dose-rate has been defined and estimated here no more has been postulated than that Eq. 8 should hold true for a sufficiently long pulse or for a pulse in which every part can be considered to act quasi-stationarily.

Appendix

Under equilibrium conditions the ion distribution in the chamber has to satisfy the following conditions

$$\operatorname{div}(n^+ u^+ \mathbf{E}) = -\operatorname{div}(n^- u^- \mathbf{E}) = q - \alpha n^+ n^- \quad \ldots\ldots\ldots\ldots (20)$$

where $\mathbf{E}$ is the vector of the electric field strength. To these equations may be added

$$\operatorname{div} \mathbf{E} = \varrho = e\,(n^+ - n^-) \quad \ldots\ldots\ldots\ldots\ldots\ldots (21)$$

$$\mathbf{i} = e\,\mathbf{E}\,(n^+ u^+ + n^- u^-) = \text{const} \quad \ldots\ldots\ldots\ldots\ldots (22)$$

In the one-dimensional case all these equations can be replaced by the following (Thomson (11))

$$\frac{u^+ u^-}{e\,(u^+ + u^-)} \frac{d}{dx}\left(E \frac{dE}{dx}\right) = q - \frac{\alpha}{e^2 E^2 (u^+ + u^-)^2}\left(i + u^- E \frac{dE}{dx}\right)\left(i - u^+ E \frac{dE}{dx}\right) \quad \ldots\ldots (23)$$

In the cylindrical case (SEELIGER (7)) we find the same expression if we write rE, rdr and ri instead of E, dx and i, i no longer being constant.

A good approximation of Eq. 22 in the one-dimensional case has been given by THOMSON, who writes the chamber characteristic (under the assumption that $n^+ = n^-$) as

$$V = Ri\sqrt{\frac{I}{I-i}} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (24)$$

where I_s is the saturation value of the current. We can solve i and express ε as

$$\varepsilon = 1 - \frac{i}{I} = 1 + x - \sqrt{x(2+x)} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (25)$$

where

$$x = \frac{V^2}{2R^2I^2} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (26)$$

and for small values of ε

$$\varepsilon \approx \frac{1}{2x} = \frac{R^2I^2}{V^2} = \text{const} \times \frac{1}{V^2} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (27)$$

i. e. we have derived Eq. 8, which is also identical with the approximate equation given by BOAG and WILSON (3).

To determine the value of the constant, an approximate expression for small values of ε is most easily derived in another way. If the recombination is small, we can first omit the corresponding term in Eq. 20 and for the one-dimensional case after integration get

$$n^+ = \frac{q}{u^+E}x, \qquad n^- = \frac{q}{u^-E}(d-x) \quad \ldots\ldots\ldots\ldots\ldots \quad (28)$$

If we assume this ion distribution to be true approximately also for a certain recombination the current can be obtained by a volume integration from Eq. 20

$$i(x) = i^+ + i^- = \text{const} = i^+(d) = e\int_s \text{div}\,(n^+u^+\mathbf{E})\,dS = e\int_s qdS - e\int_s \alpha n^+n^-dS \quad . \quad (29)$$

and

$$\varepsilon = \frac{\Delta i}{i} = \frac{\int_s \alpha n^+n^-dS}{\int_s qdS} = \frac{\int_0^d \alpha n^+n^-dx}{\int_0^d qdx} = \frac{1}{6}\frac{\alpha q d^4}{u^+u^-V^2} \quad \ldots\ldots\ldots\ldots \quad (30)$$

Hence, if $u^+ \approx u^-$, x can be obtained from

$$\frac{1}{2x} = \varepsilon \approx \frac{2}{3}\frac{\alpha q d^4}{(u^+ + u^-)^2} \times \frac{1}{V^2} \quad \ldots\ldots\ldots\ldots\ldots \quad (31)$$

Finally, the mean value of ε (for a constant dose-rate) can be calculated as

$$\bar{\varepsilon} = \frac{\int_0^\tau \varepsilon(t)\,j(t)\,dt}{\int_0^\tau j(t)dt} = \frac{1}{\tau}\int_0^\tau \varepsilon(t)\,dt = \frac{1}{\tau} \times \frac{\text{const}}{V_0^2}\int_0^\tau \frac{dt}{(1-at)^2} =$$

$$= \frac{\varepsilon_0}{1-a\tau} = \varepsilon_0 \times \frac{V_0}{V_\tau} = \sqrt{\varepsilon_0\varepsilon_\tau} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (32)$$

SUMMARY

The author gives a survey of the possibilities of determining the ionization losses caused by ion recombination in thimble chambers irradiated with roentgen rays of very high intensity. Dose measurements have been made, and saturation curves are shown illustrating the performance of two common types of chambers irradiated with short roentgen pulses from the discharge tube earlier described by SIEVERT. In a small volume it is possible to deliver with this tube roentgen doses up to 1,000 r with dose-rates up to 10^7 r/sec, the pulse duration being shorter than 100 μs. It is shown that, even at these high dose-rates, the saturation in the chambers can easily be determined by help of the common formulae used at moderate dose-rates. A method is suggested for calculating the real dose, when the dose-rate is not known sufficiently well to permit a direct estimation of the correction that should be applied to the measured values because of the ion recombination.

ZUSAMMENFASSUNG

Der Verfasser gibt eine Übersicht über die Möglichkeiten Ionisationsverluste, die durch Rekombination in Kleinkammern bei der Messung von Röntgenstrahlen von hoher Intensität entstehen, zu bestimmen.

Dosismessungen wurden durchgeführt und die Sättigungskurven zeigen das Verhalten zweier Kammertypen, die mit Röntgenstrahlen von der von SIEVERT früher beschriebenen Entladungsröhre bestrahlt werden.

In einem kleinen Volumen ist est möglich mit dieser Röhre Röntgendosen bis zu 1,000 r mit Dosisleistungen bis zu 10^7 r/sek., entsprechend einer Bestrahlungszeit von weniger als 100 μs zu erhalten.

Es wird gezeigt dass auch bei diesen hohen Dosisleistungen die Sättigung in der Kammer leicht bestimmt werden kann mit Hilfe der gewöhnlichen Formeln für mittlere Dosisleistungen. Eine Methode wird vorgeschlagen zu Berechnung der wirklichen Dosis, wenn die Dosisleistung nicht genügend bekannt ist um den durch die Rekombination hervorgemessenen Korrektionsfaktor direkt zu bestimmen.

RÉSUMÉ

L'auteur donne un aperçu des possibilités de déterminer les pertes d'ionisation dues à la recombinaison des ions dans les chambres «en dé à coudre» irradiées par des rayons roentgen de très haute intensité. Des mesures de doses ont été effectuées; les courbes de saturation sont présentées, montrant le rendement de deux types courants de chambres recevant de courtes impulsions de rayons roentgen émises par le tube à décharge décrit par SIEVERT.

Il est possible, avec ce tube, d'émettre dans un petit volume des doses roentgen allant jusqu'à 1,000 r, avec un débit s'élevant à 10^7 r/sec, la durée de l'impulsion étant inférieure à 100 μs. L'auteur montre que, même avec ces hauts débits, il est facile de déterminer la saturation des chambres grâce aux formules habituelles employées avec des débits modérés. Il suggère une méthode pour calculer la dose réelle, quand on ne connait pas le débit avec assez de précision pour pouvoir estimer directement la correction qui doit être appliquée aux valeurs mesurées en raison de la recombinaison des ions.

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BOOK REVIEWS

DIAGNOSIS AND LOCALIZATION OF BRAIN TUMORS. By George E. Moore, 271 pages, 87 illustrations, Charles C. Thomas, Springfield, Ill. 1953. $ 10: 50.

The author is the pioneer in the field which is the scope of this volume. In March 1947, he succeeded for the first time in staining a brain tumour with fluorescein. At that time, he was ignorant of former studies of the blood-brain barrier. Various pathologic conditions, especially tumours, may cause local damage to this barrier, thus permitting negatively-charged particles, of which fluorescein is one, to permeate the damaged area.

MOORE was the first to put this phenomenon to practical use, and in his book he accounts for 500 cases in which fluorescein has been given preoperatively. Small samples obtained by aspiration through a needle inserted into deeply situated tumours fluoresced clearly in ultra-violet light with very few exceptions. At his hospital, this has been the routine method for detecting and limiting sub-surface tumours at operation, but as far as the reviewer knows, has practically never been used elsewhere. This is probably due to that the fluorescence is easily obscured by blood and brain tissue traumatized earlier in the operation and the method has thus a very limited value for studying the tumour in the operating field.

The author discusses the possibility of the vital staining of tumours and making them radiopaque and finds that these problems may be insoluble at the present time. MOORE's attempts to use fluorescein as the carrier of a gamma-ray emitting isotope resulted in diiodofluorescein tagged with I^{131}. With this substance he has studied the blood-brain barrier using experimental brain tumours in mice, as well as the fate of the substance in the body. The main problem is, of course, the detection of pathologic intracranial conditions by means of radioactive measurements on the unbroken skull. Various physical and geometric problems in such counting are discussed, including brain phantom studies. MOORE's conclusions seem in the main to be sound. He further reports on the search for substances other than $DI^{x}F$, and announces the first promising results with iodized human serum albumin (Risa), and sodium iodide after the blocking of the thyroid with previously administered iodine. In an addendum, apparently written a year-and-a-half after the main part of the book, the author returns to these methods and to technical problems concerning equipment, positioning, etc. The employment of Risa seems to indicate progress with a higher differential and longer lasting uptake in the tumours.

The book is stimulating, and the author does not hesitate to tackle great and difficult problems. It seems a pity, then, that this assessment cannot be said to hold good for the entire volume. The 500 cases of brain tumours which the author has studied with $DI^{x}F$ are not accounted for in such a manner that the reader can judge the results for himself; this is a prerequisite which one has every right to demand in a scientific publication. No reason is stated why only some of the cases are tabulated. In the table which is labelled "Correctly Localized Tumours" and consisting of only 17 cases, at least three were wrongly localized, *e. g.* in the frontal instead of the temporal lobe. From a neuroradiologic standpoint, such localization would definitely have been classified as incorrect. Two or three more cases are impossible to judge. The author deserves credit for his criticism of the statistical results claimed by other authors, which have been obtained through a combination of clinical and isotopic diagnoses. The author seems to lack knowledge of modern neuroradiology and to share this failing with the author of the foreword. The roentgen reports of the few case-histories included indicate a considerable lack of diagnostic stringency. These conditions may be accounted for by the fact that the author does not attempt to compare the isotopic with roentgenologic methods of diagnosis and localization.

The reader cannot, however, avoid considering the possible future importance of the isotopic methods. Their employment for localization in cases with definite brain tumours can be permitted only for scientific purposes. Even the best isotopic method cannot give more than a geometric localization, and the preoperatively needed information is the topography of the tumour, the part of the brain in which it is growing, whether it is infiltrating or not, its relation to displaced ventricles, vessels, etc., and if possible, its nature. For this last purpose it is possible that in the future one isotopic method or another will be useful, particularly in those few cases in which it is uncertain whether a change demonstrated in pneumography or angiography is due to a tumour or an abnormality. If the radioactive tracer method can be developed to the point where it can be used as the only method to classify uncertain cases it will certainly, in the reviewer's opinion, have achieved its greatest usefulness.

Sven Erik Sjögren.

SCHICHTBILDER VON BRONCHIALVERÄNDERUNGEN BEI DER LUNGENTUBERKULOSE. Von H. Blaha. 113 pages, 47 illustrations. George Thieme Verlag, Stuttgart 1954. Dm. 18: —.

By way of introduction, the author points out the importance of diagnosing bronchial changes in tuberculosis. Certain of these changes exclude treatment by collapse of the lung whereas others indicate a resection.

It is by reason of the intimate connection between the changes in the parenchyma and bronchi that the author prefers tomography. Neither bronchoscopy or bronchography, as distinguished from tomography, give information concerning the parenchyma and the bronchi at the same time. Bronchoscopy and tomography complement each other and the latter should afford guidance for the bronchoscopy which follows.

The author employs practically only the frontal tomogram with smaller variations of adjustment. The movement of the tube is cranio-caudal, corresponding with the long axis of the body of the patient. The author points out the limitation of tomography in this form but states that the cases presented have to a large extent been selected by degrees from resection material. Tomography has thus proved applicable in a form suitable for routine work.

Some fifty cases are presented as examples of the suitability of employing the tomographic method in tuberculous bronchial changes. The tomograms are in the majority of cases correlated to the bronchogram, the bronchoscopic findings and the pathologico-anatomic investigation of the resection preparation.

Radiologically, changes may be observed: 1. In the course of the bronchi. 2. In their form: constrictions, dilatation, etc. 3. In the thickness and contour of the wall of the bronchus.

Good agreement exists between these observed changes and the findings after resection. Whether there is a specific or unspecific change can, however, only be decided by histologic examination.

A copious illustrative material has been included partly in the form of tomograms, partly of comparative bronchograms and illustrations of resection material. The majority of the tomograms in spite of difficulties in reproduction are of good quality. A number of explanatory arrows or sketches, however, in the opinion of the reviewer, appear desirable. Some of the less happy reproductions might be left out with advantage.

The material presented gives a good conception of the suitability of the tomographic method in studies of the bronchi. However, the author's belief that the differentiation between a tuberculous stenosis and a bronchial carcinoma may be made with fairly great certainty is not shared by the reviewer.

In order to exploit the tomographic method to the full, the reviewer feels tomography in the lateral plane as well as in suitable oblique projections should also be employed.

Herman Lodin.